SOCIAL DETERMINANTS OF END-STAGE RENAL DISEASE

ALAN CASS

MBBS, BA, FRACP, Grad. Dip. Clinical Epidemiology

A thesis submitted in fulfilment of the requirements for the degree of

Doctor of Philosophy, University of Sydney

Department of Public Health and Community Medicine, University of Sydney

Menzies School of Health Research, Darwin, Northern Territory

September, 2002

DECLARATION

I hereby certify that the work embodied in this thesis is the result of original research and is not being submitted for a higher degree to any other university or institution.

Alan Cass 4/9/2002

Alan Cass Date

AUTHOR'S CONTRIBUTION

The work presented in this thesis has been carried out by the author under the supervision of Associate Professor Joan Cunningham, Menzies School of Health Research, and Dr Wendy Hoy, Menzies School of Health Research. This included: planning of research, design of component studies, ethics committee submission, the collection, management, analysis and interpretation of data, writing of manuscripts for submission to peer-reviewed journals, and the writing of the thesis, with the exception of aspects of the research specified below.

Chapter seven presents the findings of a collaborative, multidisciplinary research project undertaken in the Royal Darwin Hospital Renal Unit under the auspices of the Cooperative Research Centre for Aboriginal and Tropical Health (CRCATH). Dr Anne Lowell was the project coordinator and responsible for the collection and analysis of qualitative data. The author was a member of the core research team and responsible for the writing and submission of the manuscript arising from this research.

The data analysed in this thesis were from existing national datasets with additional primary data gathered by the author. The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) provided a raw national dataset, for all patients who commenced renal replacement therapy (RRT) in Australia during 1993-1998, that included variables specified by the author. The Australian Bureau of Statistics provided selected area-level demographic and socio-economic data from the 1996 Census. Primary data were collected from every Australian renal unit providing treatment for Indigenous patients, regarding the place of usual residence of their Indigenous patients prior to commencement of RRT.

The appendices represent research separate to, but derived from this thesis. Appendices 1 and 2 include further research into the screening and

management of chronic renal insufficiency in general practice. Appendix 2 is the result of collaboration with Tim Usherwood, Professor of General Practice, University of Sydney at Westmead Hospital. Appendices 3 and 4 include further research into renal disease mortality in Australia. These studies were conceived and supervised by the author, but carried out by Shu Qin Li, in partial fulfilment of the requirements of the degree of Master of Public Health, Northern Territory University.

ETHICS CLEARANCE

The studies described in this thesis were approved by the Joint Institutional Ethics Committee of the Menzies School of Health Research and Royal Darwin Hospital, and the Ethics Committee of the Northern Territory University. For the study described in chapter seven, individual participants provided oral and written consent, obtained in their first language, to participate in the research.

The data reported here have been supplied by the Australia and New Zealand Dialysis and Transplant Registry. Registry approval was obtained for all relevant analyses. The interpretation of these data is the responsibility of the author and should in no way be seen as an official policy or interpretation of the Australia and New Zealand Dialysis and Transplant Registry.

ABSTRACT

Introduction

In this thesis I explore the social determinants of end-stage renal disease (ESRD) in Australia, with a focus on renal disease among Indigenous Australians. This body of research describes regional patterns in the incidence of ESRD among Indigenous and non-Indigenous Australians; the relationship between the incidence of ESRD and regional level markers of socioeconomic disadvantage; the long-term effect of delayed referral to nephrology care on ESRD treatment outcomes; the relationship between delayed referral and regional level markers of socioeconomic disadvantage; the effect of miscommunication on the delivery of renal care to Indigenous Australians; Indigenous Australians' access to renal transplantation compared with non-Indigenous Australians; and proposes a new explanatory model for the excess burden of renal disease in indigenous populations.

ESRD incidence

Marked regional variation in the incidence of ESRD among Indigenous Australians is demonstrated using Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) data regarding 719 Indigenous Australians who commenced ESRD treatment during 1993 to 1998. Standardised ESRD incidence is highest in remote regions, where it is up to 30 times the national incidence for all Australians. Area-based measures of disadvantage are strongly associated with the regional incidence of ESRD in Indigenous Australians. (Early school leavers $r = 0.68$, $p < 0.001$; unemployment rate $r = 0.72$, $p < 0.001$; median household income $r = -0.71$, $p < 0.001$; number of persons per bedroom $r = 0.84$, $p < 0.001$; and low birth weight $r = 0.49$, $p = 0.003$.)

Significant variation in the incidence of ESRD within Australian capital cities is demonstrated using ANZDATA data regarding 5,013 patients (97% non-

Indigenous) who commenced ESRD treatment during 1993 to 1998. There is a significant correlation ($r = -0.41$, $p = 0.003$) between the standardised incidence ratio for ESRD and the Index of Relative Socio-Economic Disadvantage, an index developed by the Australian Bureau of Statistics to describe the socio-economic characteristics of an area. Capital city areas that are more disadvantaged have a higher incidence of ESRD.

Delayed referral for nephrology care

Late referral to a nephrologist, defined in this thesis as commencement of dialysis within three months of referral, has been associated with increased early morbidity and mortality on ESRD treatment. In this thesis I examine the influence of late referral on the long-term likelihood of receiving a transplant and mortality, and examine the relationship between late referral and socio-economic disadvantage.

Late referral was associated with increased mortality (adjusted hazard ratio 1.19, 95% CI 1.04–1.35) and decreased likelihood of receiving a transplant (adjusted rate ratio 0.78, 95% CI 0.64–0.95) beyond the initial year of renal replacement therapy. The proportion of ESRD patients referred late varied between capital city areas and was significantly higher in areas of greater disadvantage. Indigenous ESRD patients were significantly more likely to be referred late.

Miscommunication between Indigenous ESRD patients and health care workers

In chapter seven, I identify factors limiting the effectiveness of communication between Indigenous ESRD patients and health care workers. The research demonstrated that miscommunication was pervasive and often went unrecognised by both patients and staff. A shared understanding of key concepts relating to diagnosis, prevention of progression of renal disease and ESRD treatment was rarely achieved. Strategies for improving communication are suggested and are the focus of ongoing research.

Inequitable access to renal transplantation

In this thesis I assess Indigenous Australians' access to renal transplantation, compared with non-Indigenous Australians; and examine whether disparities are due to a lower rate of acceptance onto the waiting list and/or a lower rate of moving from the waiting list to transplantation. Indigenous patients had a lower transplantation rate (adjusted Indigenous:non-Indigenous rate ratio 0.32, 95% CI 0.25–0.40). They had both a lower rate of acceptance onto the waiting list (adjusted rate ratio 0.50, 95% CI 0.44–0.57) and a lower rate of moving from the waiting list to transplantation (adjusted rate ratio 0.50, 95% CI 0.38–0.65). The disparities were not explained by differences in age, sex, co-morbidities or cause of renal disease.

Conclusion and new explanatory model for the excess burden of renal disease in indigenous populations

In the Australian context, regional patterns of ESRD incidence and access to renal treatment have not been established previously. The importance of social, economic and cultural determinants of renal disease is not known. These are the key questions addressed in this thesis.

Previous explanations for the excess burden of renal disease in Indigenous populations can be categorised as: 1) the primary renal disease explanation; 2) the genetic explanation; 3) the early development explanation; and 4) the socio-economic explanation. In this thesis I propose a new model which integrates the existing evidence. This model can be used to illuminate the pathways between disadvantage and the human biological processes which culminate in ESRD, and to propose prevention strategies across the life-course of Indigenous Australians to reduce their ESRD risk. The model is likely to be relevant to an understanding of patterns of renal disease in other high-risk populations. Furthermore, similar pathways might be relevant to other chronic diseases, such as diabetes and cardiovascular disease, among

indigenous populations throughout the developed world and to the populations of developing countries.

ACKNOWLEDGEMENTS

My supervisors, Joan Cunningham and Wendy Hoy, provided the support, enthusiasm and expertise required to guide this thesis. Wendy Hoy provided the inspiration and resources to enable me to uproot my family from Sydney in order to pursue this research 3,500 kilometres away in Darwin. Joan Cunningham provided crucial input at every stage and has guided me and collaborated in the broadening of the scope of my research from clinical science to social science.

Many people at the Menzies School of Health Research, the Cooperative Research Centre for Aboriginal and Tropical Health, and Royal Darwin Hospital collaborated in this research. Zhiqiang Wang gave wise counsel and assistance with data management and statistical issues, Paul Snelling discussed research ideas over many cups of coffee, Gurmeet Singh shared a phone extension and stories of research and clinical work over a corral divider, Anne Lowell and Michael Christie provided critical insights into issues of cross-cultural communication.

Rod Silburn at the Australian Bureau of Statistics searched far and wide for published datasets in order to reduce costs of purchasing census data. Brian Livingstone at ANZDATA discussed issues relating to data collection and validity and responded to multiple requests with efficiency and good cheer. Peter Day at the National Perinatal Statistics Unit gave great assistance in accessing data. Professor John Horvath at Royal Prince Alfred Hospital provided enthusiastic support and advice throughout.

This work was supported financially by the Centre for Kidney Research at the Children's Hospital, Westmead, through John Knight and also by the Colonial Foundation. The Cooperative Research Centre for Aboriginal and Tropical Health, especially through the efforts of Michael Duffy, supported the

dissemination of research findings, and also directly funded the research described in chapter seven.

My father-in-law, Peter Arnold, critically edited all the manuscripts for publication. This work could not have been completed without his efforts. My mother, Bettina Cass, provided critical input. I thank my wife Lauren for allowing me to return to work after the children's bedtime, several nights per week for many months and for encouraging me throughout to pursue my research interests from Sydney to the tropical north and beyond.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

PUBLICATIONS ARISING FROM THE THESIS

Some of the original material presented in this thesis has been published in peer-reviewed journals. The remainder has been submitted for publication.

Chapter 2. **Cass A**, Cunningham J, Wang Z, Hoy W. Regional variation in the incidence of end-stage renal disease in Indigenous Australians. *Medical Journal of Australia* 2001; 175 (1): 24-27.

Chapter 3. **Cass A**, Cunningham J, Snelling P, Wang Z, Hoy W. End-stage renal disease in Indigenous Australians: a disease of disadvantage. *Ethnicity and Disease* 2002; 12 (3): 373-378.

Chapter 4. **Cass A**, Cunningham J, Wang Z, Hoy W. Social disadvantage and variation in the incidence of end-stage renal disease in Australian capital cities. *Australia and New Zealand Journal of Public Health* 2001; 25 (4): 322-326.

Chapter 5. **Cass A**, Cunningham J, Arnold P, Snelling P, Wang Z, Hoy W. Delayed referral to a nephrologist: Outcomes among those who survive at least one year on dialysis. *Medical Journal of Australia* 2002; 177 (3): 135-138.

Chapter 6. **Cass A**, Cunningham J, Snelling P, Wang Z, Hoy W. Urban disadvantage and delayed nephrology referral in Australia. *Health and Place*. In press.

Chapter 7. **Cass A**, Lowell A, Christie M, Snelling P, Flack M, Marrnganyin B, Brown I. Sharing the true stories: improving communication between Aboriginal patients and health carers. *Medical Journal of Australia* 2002; 176 (10): 466-470.

Chapter 8. **Cass A**, Cunningham J, Snelling P, Wang Z, Hoy W. Renal transplantation for Indigenous Australians: Identifying the barriers to equitable access. Submitted May 2002 *Ethnicity and Health*.

Chapter 9. **Cass A**, Cunningham J, Snelling P, Wang Z, Hoy W. Exploring the pathways from disadvantage to end-stage renal disease. Submitted August 2002 *Social Science and Medicine*.

Appendix 1. **Cass A.** Kidney disease: are you at risk? (Editorial) *Medical Journal of Australia* 2002; 176 (11): 515-516.

Appendix 2. Usherwood T, **Cass A.** Early renal impairment: the role of the general practitioner. *Medicine Today.* In press.

Appendix 3. Li SQ, Cunningham J, **Cass** A. Renal-related deaths in Australia, 1997-1999. Submitted August 2002 *American Journal of Kidney Disease.*

Appendix 4. Li SQ, **Cass A**, Cunningham J. Cause of Death in Patients with End Stage Renal Disease: Assessing Concordance of Death Certificates with Registry Reports. Submitted August 2002 *Australia and New Zealand Journal of Public Health.*

Other publications and reports:

Cass A, Cunningham J, Hoy W. The relationship between the incidence of end-stage renal disease and markers of socio-economic disadvantage. *New South Wales Public Health Bulletin.* In press.

Cass A, Snelling P, Cunningham J, Wang Z, Hoy W. Timing of nephrology referral: a study of its effects on the likelihood of transplantation and impact on mortality. *Nephrology* 2002; 7: S29-S32.

Knight J, **Cass A.** A national early renal impairment task force: Discussion paper–November 2000, submitted to the Australian Kidney Foundation and the Australia and New Zealand Society of Nephrology.

CHAPTER 1: INTRODUCTION

Renal disease has a profound impact on indigenous individuals and communities. In the Australian context, regional patterns of ESRD incidence and access to renal treatment have not previously been established. The importance of social, economic and cultural determinants of renal disease is not known.

Previous Australian studies of renal disease epidemiology have generally been limited to a description of differences according to age, sex, cause of renal disease or 'race'. Patterns of incidence of renal disease and access to services have been analysed at the national or state level. In this thesis, I have analysed regional patterns of incidence of ESRD and of access to treatment services. I also describe their relationship to socioeconomic and cultural factors.

This body of research describes regional patterns in the incidence of ESRD among Indigenous and non-Indigenous Australians; the relationship between the incidence of ESRD and regional level markers of socioeconomic disadvantage; the long-term effect of delayed referral to nephrology care on ESRD treatment outcomes; the relationship between delayed referral and regional level markers of socioeconomic disadvantage; the effect of miscommunication on the delivery of renal care to Indigenous Australians; and inequitable access to renal transplantation for Indigenous Australians. As a result of my findings, I propose a new explanatory model for the excess burden of renal disease in indigenous populations.

Previous explanations for the excess burden of renal disease in Indigenous populations can be categorised as: 1) the primary renal disease explanation; 2) the genetic explanation; 3) the early development explanation; and 4) the socio-economic explanation. I discuss the strengths and weaknesses of these explanations and propose a new model which integrates all the existing evidence. I use the model to illuminate the pathways between disadvantage and the human biological processes which culminate in ESRD, and also to

propose prevention strategies across the life-course of Indigenous Australians to reduce their ESRD risk.

CHAPTER 2: REGIONAL VARIATION IN THE INCIDENCE OF END-STAGE RENAL DISEASE IN INDIGENOUS AUSTRALIANS

Publication details:
Cass A, Cunningham J, Wang Z, Hoy W. Regional variation in the incidence of end-stage renal disease in Indigenous Australians. *Medical Journal of Australia* 2001; 175 (1): 24-27.

2.1: Abstract

Objective: To evaluate regional variation in the incidence of end-stage renal disease (ESRD) in Indigenous Australians. To examine proximity to ESRD treatment facilities for Indigenous patients.

Design: Secondary data review with collection of primary data regarding place of residence before commencement of renal replacement therapy.

Participants: Indigenous ESRD patients who commenced treatment in Australia during 1993–1998.

Methods: We obtained data from the Australian and New Zealand Dialysis and Transplant Registry regarding 719 patients who started ESRD treatment between 1 January 1993 and 31 December 1998. We obtained primary data from the treating renal units to determine the place of residence before commencement of renal replacement therapy. We calculated the average annual incidence of ESRD for each of the 36 Aboriginal and Torres Strait Islander Commission regions using 1996 Census-based population estimates. We calculated standardised incidence ratios with 95% confidence intervals for each region. We compared the number of cases with the treatment facilities available in each region.

Main Outcome Measure: Regional standardised ESRD incidence for Indigenous Australians referenced to the total resident population of Australia.

Results: Standardised ESRD incidence among Indigenous Australians is highest in remote regions, where it is up to thirty times the total national incidence. In urban regions the standardised incidence is much lower, but remains significantly higher than the total national incidence. Forty-eight percent of Indigenous ESRD patients come from regions without dialysis or transplant facilities and 16.3% from regions with only satellite dialysis facilities.

Conclusions: There is marked regional variation in the incidence of ESRD among Indigenous Australians. Because of the location of treatment centres, there is inequitable access to ESRD treatment services for a significant proportion of Indigenous patients.

2.2: Introduction

In Australia geographical differentials in morbidity and mortality have been demonstrated.[1-4] In general, people living in rural and remote areas have *higher death rates and hospital separation rates, which have been attributed* to socio-economic status,[1,3-5] access to health services,[2,6,7] ethnicity[4] and racial discrimination.[8] Indigenous Australians constitute a disproportionate number of new patients commencing end-stage renal disease (ESRD) treatment.[9] In 1997, the age and sex adjusted incidence rate for Indigenous Australians starting ESRD treatment was nearly nine times that of non-Indigenous Australians.[10] Although epidemics of renal disease among Aborigines in defined areas[11] have been documented, there have been no systematic reports of the regional patterns of ESRD incidence in Australia. In this study we have attempted to determine these patterns and to examine accessibility of ESRD treatment locations for Indigenous patients.

2.3: Methods

Databases

The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) maintains a database of patients treated by maintenance dialysis or renal transplantation in Australia. All renal units that provide ESRD treatment in Australia participate in the Registry. Postcode of residence at the start of treatment is collected for all new patients entered into the ANZDATA Registry. ANZDATA maintains a list of hospital renal transplant services, tertiary referral units and satellite dialysis units. Satellite units are defined as dialysis facilities, generally staffed by specialist nurses, which are geographically separate from hospital nephrology services.

Data validity

Postcode of residence at the start of treatment is an imperfect indicator of the usual place of residence before starting treatment. In remote areas a single postcode may apply to many communities across a vast area. Furthermore, patients may be required to relocate to a major regional centre to access dialysis services; thus their postcode at the start of treatment may not reflect their previous usual place of residence. To determine the usefulness of postcode data, we reviewed 104 Indigenous patients who commenced ESRD treatment from 1993 to 1998 at Royal Darwin Hospital. For these patients the previous usual place of residence was known. Fifty-one Indigenous patients (49.0%) had postcodes in the Darwin region, but only 9 of these 51 patients previously lived in this region. The other 42 had relocated to Darwin to commence dialysis and were from communities across the Top End, extending from the Torres Strait in Queensland to Geraldton in WA. As a result of this audit, we decided to collect primary data from each treating renal unit regarding the previous place of usual residence of their Indigenous patients.

Indigenous identification was based upon self identification and discussion with the treating physician. There is often significant concern about the quality of Indigenous identification in morbidity, mortality and demographic data sets. However, we believe that identification in the ANZDATA registry is good. A survey form is filled in every six months for all patients on maintenance dialysis or with functioning transplants. Question five is about "Racial origin" and includes a prompt regarding Aboriginality. ESRD patients have regular contact with renal services from the time of diagnosis, through intensive maintenance therapy until death. There is heightened awareness of Aboriginal renal disease and multiple opportunities exist to reconfirm data accuracy.

Patients

From 1 January 1993 to 31 December 1998, 719 Indigenous patients started treatment in Australia. We determined the previous place of usual residence for 680 (94.6%). For 38 patients (5.3%) we used the postcode at entry as an indicator of previous place of usual residence. No geographical data were obtainable for one patient.

Geography

We used the 36 Aboriginal and Torres Strait Islander Commission (ATSIC) regions (Table 2.1 and Figure 2.1) as our geographic units for analysis. These are legally prescribed administrative areas and the smallest geographical areas for which accurate resident population estimates for the Indigenous population are available.[12] We assigned the place of usual residence for Indigenous patients to the appropriate ATSIC regions. We assigned the 38 patients for whom we could not obtain exact information on previous place of residence to ATSIC regions according to their postcode at the time of beginning ESRD treatment, using information provided by the Australian Bureau of Statistics (ABS).

Statistical analysis

Using population estimates based on the 1996 Census, we calculated the average annual incidence of ESRD in the 36 ATSIC regions. We used ABS estimates of the Indigenous population, derived using Census information on place of usual residence. These estimates are adjusted for net census undercount and non-response to the Census question about Indigenous status.[13] We used indirect standardisation to calculate a standardised incidence ratio with 95% confidence intervals for each region. Rates for the total Australian resident population were used as the reference (standardised incidence ratio equals incidence in the Indigenous population divided by incidence in the total Australian population, after adjustment for differences in the age and sex composition of both populations). Statistical analysis was performed using Stata (Release 6.0, College Station, Texas, 1999).

Ethical approval

We obtained ANZDATA approval to analyse geographic data for Indigenous patients starting treatment for ESRD between 1 January 1993 and 31 December 1998. We also obtained approval for the study from the joint institutional ethics committee of Royal Darwin Hospital and the Menzies School of Health Research. The head of each renal unit gave written consent for us to access potentially identifying patient data in order to determine the previous place of usual residence for Indigenous ESRD patients.

2.4: Results

Mapping reveals significant variation in the incidence of ESRD among Indigenous Australians. The areas of highest incidence, up to 1300 cases per million per year, were the remote regions of Tennant Creek, Aputula and Jabiru in the Northern Territory, Warburton and Kalgoorlie in Western Australia, and Ceduna in South Australia (Figure 2.1). The areas of lowest incidence, less than 100 per million per year, were the regions of Rockhampton and Brisbane in south-east Queensland, Sydney and Queanbeyan in NSW/ ACT, Wangaratta including much of eastern Victoria and Hobart which encompasses all of Tasmania (Figure 2.1). The standardised incidence ratio for ESRD (compared to the total national population incidence) ranged from less than two in Rockhampton, Sydney, Queanbeyan and Wangaratta to more than twenty-five in Aputula, Kalgoorlie and Tennant Creek (Table 2.1). There were no ESRD cases identified as Indigenous in Tasmania in the six-year period.

Tertiary renal services, particularly transplant services, are located within significant population centres such as capital cities. Three hundred and forty-five (48.0%) Indigenous ESRD cases occurred in ATSIC regions without ESRD treatment facilities (Table 2.1). A further 117 (16.3%) occurred in regions with only satellite dialysis facilities (Table 2.1). Most Indigenous patients must travel hundreds of kilometres to access transplant services, which are located in Perth, Adelaide, Melbourne, Sydney, Newcastle and Brisbane.

2.5: Discussion

In this study we have demonstrated a large gradient in Indigenous ESRD incidence from urban to remote regions and highlighted inequitable access for remote patients to treatment facilities. However, even in urban regions, the Indigenous ESRD incidence was high after age and sex standardisation. Poor Indigenous health outcomes are not confined to the most disadvantaged or most remote regions, but exist across the Indigenous population.

The quality of Indigenous identification is a concern in this study. ANZDATA relies upon self identification and discussion with the treating physician. Self identification is the method used by the Australian Bureau of Statistics in census collections and is generally used in health related data collection. We believe that the quality of identification in this study is high due to the ongoing intensive interaction of ESRD patients with medical and nursing staff, Indigenous status being a prominent question in the six monthly survey form, and the strong awareness of Indigenous ESRD among nephrologists. The most likely error would be the failure to identify all urban Indigenous ESRD patients. This would result in an underestimate of the true Indigenous ESRD incidence in urban areas and an overestimate of the gradient from urban to remote Indigenous ESRD incidence. Yet, as this gradient is so large, representing an almost 20-fold variation in standardised ESRD incidence, it can not be entirely explained by problems with Indigenous identification. The very high standardised incidence ratios for Indigenous people in remote areas would not change.

These results have significant implications for the delivery of services to Indigenous people with ESRD. Satellite facilities opened in the Jabiru region in 1999 and the Katherine region in 2000 (after the patients in this study commenced treatment). Of the sixteen regions with the highest Indigenous ESRD incidence, at the beginning of 2001 only Kalgoorlie, Jabiru (Tiwi Islands), Geraldton, Katherine and South Hedland have satellite dialysis units. A satellite unit is scheduled to open soon in Broome and recommendations

have been accepted to establish a satellite haemodialysis service in the Torres Strait as part of the recent Queensland Renal Strategy.[14] We recognise the significant difficulties related to the establishment and maintenance of renal treatment facilities in remote locations. These include high construction costs, poor reliability of electricity and water supply, variable water quality, difficulties in training and retaining specialised nursing staff, infrequent access to medical staff and provision of housing for patients returning to live in their local community. Despite these difficulties, treatment facilities have been established in some of the most remote communities in Australia.

Even with the availability of satellite units, initiation of ESRD treatment usually requires a prolonged stay in a major urban centre. During this stay, vascular or peritoneal access for dialysis is created, the patient starts and is stabilised on treatment and learns skills required for self care in order to return to a remote satellite dialysis unit. We should develop more innovative methods of patient education, training for self-care and delivery of treatment to allow patients to remain within their communities whenever possible. Improving prevention and treatment services in high-incidence areas should be a priority.

Indigenous people living in remote communities demand more equitable access to dialysis services,[15] regardless of practical problems related to the establishment of remote treatment facilities. The need to relocate to distant urban areas to access treatment affects the patient, patient's family and community. A recent study of ESRD among Aboriginal people of central Australia concluded:[16] "This level of illness and death (due to ESRD) represents Aboriginal family trauma and loss on a shocking scale, described without exaggeration as sorrows nearly every year (because) the young and the old are dying".

Table 2.1: End-stage renal disease cases among Indigenous Australians from 1993 to 1998

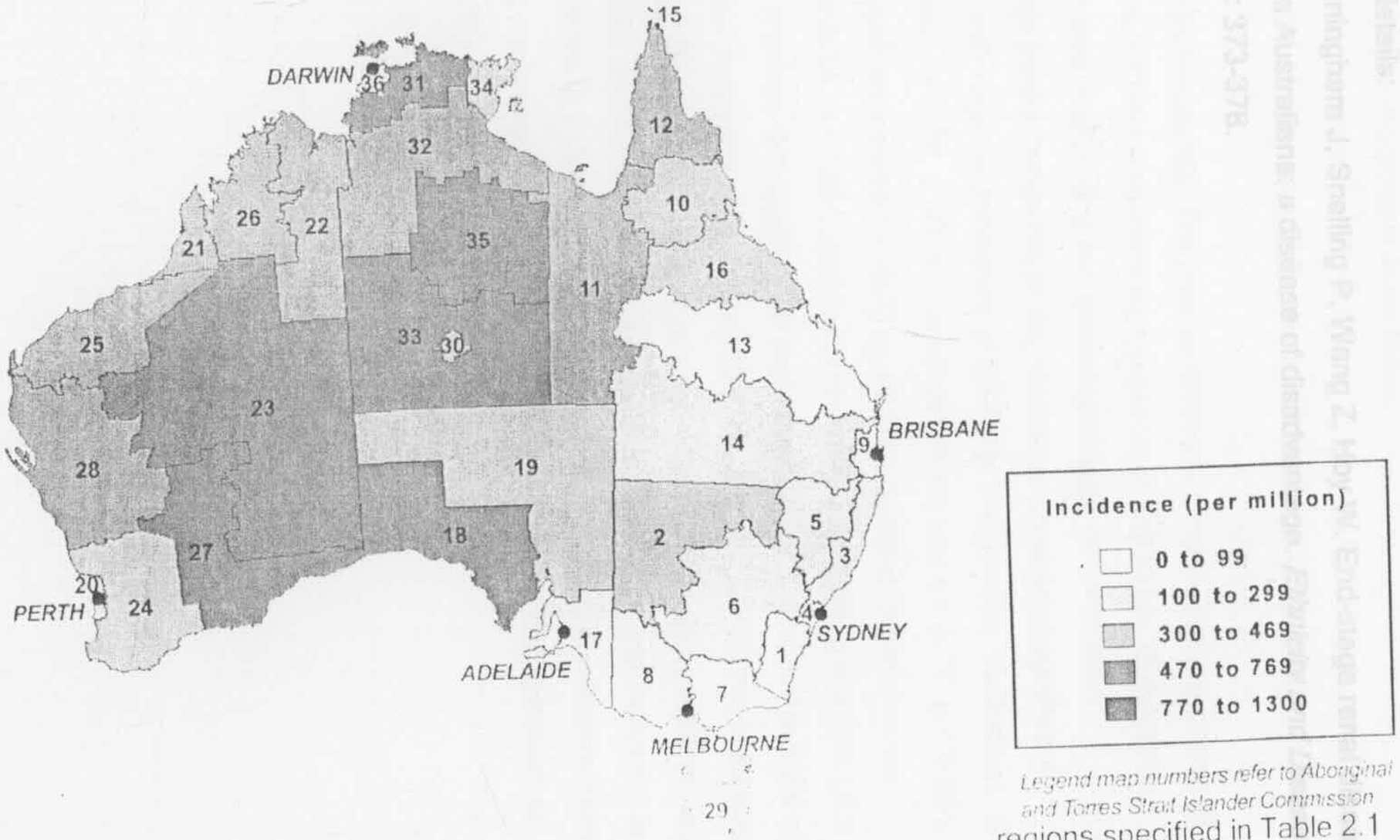
ATSIC Region (map references)	Treatment facilities†	Patients (number)	Standardised Incidence ratio* (95% CI)
Tennant Creek (35)		30	31.05 (20.96 - 44.33)
Kalgoorlie (27)	S	23	27.75 (17.60 - 41.64)
Aputula (33)		58	25.03 (19.01 - 32.36)
Warburton (23)		20	22.77 (13.91 - 35.17)
Ceduna (18)		10	22.48 (10.78 - 41.34)
Jabiru (31)		45	21.87 (15.95 - 29.26)
Geraldton (28)	S	25	18.20 (11.78 - 26.86)
Mount Isa (11)		33	17.74 (12.21 - 24.91)
Kununurra (22)		22	16.85 (10.56 - 25.51)
Katherine (32)		30	15.64 (10.56 - 22.33)
Torres Strait (15)		28	14.99 (9.96 - 21.66)
South Hedland (25)	S	18	14.75 (8.74 - 23.30)
Derby (26)		16	13.40 (7.66 - 21.76)
Nhulunbuy (34)		21	11.74 (7.27 - 17.94)
Cooktown (12)		21	11.61 (7.19 - 17.75)
Broome (21)		11	11.47 (5.73 - 20.53)
Port Augusta (19)	S	17	10.45 (6.09 - 16.74)
Bourke (2)	S	21	10.16 (6.29 - 15.53)
Townsville (16)	T, S	35	9.41 (6.55 - 13.08)
Cairns (10)	T, S	35	8.71 (6.07 - 12.12)
Alice Springs (30)	T, S	11	8.55 (4.27 - 15.30)
Narrogin (24)	S	13	8.20 (4.37 - 14.02)
Darwin (36)	T, S	17	7.02 (4.09 - 11.24)
Perth (20)	Tx, T, S	29	6.70 (4.48 - 9.61)
Adelaide (17)	Tx, T, S	15	4.62 (2.58 - 7.61)
Tamworth (5)	T, S	12	4.18 (2.16 - 7.30)
Roma (14)	T, S	8	3.70 (1.60 - 7.28)
Coffs Harbour (3)	Tx, T, S	24	3.68 (2.36 - 5.47)

Ballarat (8)	Tx, T, S	10	3.42 (1.64 - 6.28)
Wagga Wagga (6)	T, S	14	2.98 (1.63 - 5.00)
Brisbane (9)	Tx, T, S	17	2.51 (1.46 - 4.02)
Rockhampton (13)	T, S	5	1.78 (0.58 - 4.16)
Sydney (4)	Tx, T, S	16	1.77 (1.01 - 2.88)
Queanbeyan (1)	T, S	4	1.75 (0.48 - 4.48)
Wangaratta (7)	Tx, T, S	4	1.39 (0.38 - 3.55)
Hobart (29)	T, S	0	0.00 (0.00 - 1.03)

* Indirectly standardised to the rates for the total Australian resident population.

† Tx = transplant service, T = tertiary renal unit, S = satellite dialysis unit. Geographical data were unobtainable for one patient.

Figure 2.1: Incidence of ESRD in the Indigenous population by ATSIC region



Legend map numbers refer to Aboriginal and Torres Strait Islander Commission regions specified in Table 2.1

CHAPTER 3: END-STAGE RENAL DISEASE IN INDIGENOUS AUSTRALIANS: A DISEASE OF DISADVANTAGE

Publication details:

Cass A, Cunningham J, Snelling P, Wang Z, Hoy W. End-stage renal disease in Indigenous Australians: a disease of disadvantage. *Ethnicity and Disease* 2002; 12 (3): 373-378.

3.1: **Abstract**

Objective: To determine the relation between area level indicators of socioeconomic disadvantage and the regional incidence of end-stage renal disease (ESRD) in Indigenous Australians.

Design: Ecological study.

Setting: The 36 Aboriginal and Torres Strait Islander Commission regions of Australia.

Main Outcome Measures: The relation between area-based measures of disadvantage and the standardized incidence of ESRD for 36 Australian regions was examined using non-parametric tests of correlation.

Results: Area-based measures of disadvantage showed a significant association with regional incidence of ESRD in Indigenous Australians. (Early school leavers $r = 0.68$, $p < 0.001$, unemployment rate $r = 0.72$, $p < 0.001$, median household income $r = -0.71$, $p < 0.001$, number of persons per bedroom $r = 0.84$, $p < 0.001$, and low birth-weight $r = 0.49$, $p = 0.003$.) If it were possible to improve the health of all Indigenous Australians to the level of that of the general Australian population, 87% of cases of ESRD could be avoided.

Conclusions: Socioeconomic factors appear to be strongly associated with rates of ESRD among Indigenous Australians. Therefore, reducing the burden of renal disease in Indigenous Australians is likely to require interventions addressing socioeconomic disadvantage in conjunction with biomedical interventions.

3.2: Introduction

There is strong evidence of an association between socioeconomic position and morbidity and mortality,[17] and the social gradient in the occurrence of disease progressively favours those of higher socioeconomic status.[18] Socioeconomic inequalities in the health of Australians have repeatedly been observed,[1,3,19] including in relation to cardiovascular diseases and hypertension,[1,19] but not in relation to end-stage renal disease (ESRD). Research on patterns of incidence of ESRD has generally been limited to a description of differences according to age, sex and 'race'. The focus has been on 'racial' differences in physiological and pathological responses, which are regarded as being due to genetic[20] or congenital factors, such as low birth weight.[21,22]

Indigenous Australians (Aborigines and Torres Strait Islanders) continue to experience very poor health compared to other Australians. In 1991–1996, estimated life expectancy at birth was 56.9 years for indigenous males and 61.7 years for indigenous females, compared with 75.2 years for all Australian males and 81.1 years for all Australian females.[23] Indigenous Australians constitute less than 2% of the national population, but almost 10% of new patients commencing treatment for end-stage renal disease (ESRD).[9] We have previously demonstrated a striking gradient, from urban to remote regions, in the incidence of ESRD among Indigenous Australians.[24] In this study, we examine the relation between the incidence of ESRD and area level indicators of socioeconomic disadvantage among Indigenous Australians.

3.3: Methods

Geography

We used the 36 Aboriginal and Torres Strait Islander Commission (ATSIC) regions (Figure 3.1) as our geographic units for analysis. These are legally prescribed administrative areas and are the smallest geographical areas for which accurate Indigenous Australian population estimates are available.[12]

Calculation of regional incidence and standardized ratios

The Indigenous regional ESRD incidence for the period 1993–1998 was calculated using Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) data. ANZDATA maintains a database of patients treated by maintenance dialysis or renal transplantation in Australia and New Zealand.[25] All treatment centres participate in the Registry. The only patients not registered are the few who die before being established on a maintenance dialysis or transplant program.[26] Indigenous identification is based upon self-identification and discussion with the treating physician. We used Australian Bureau of Statistics estimates of the Indigenous population, derived from 1996 Census information on place of usual residence, to calculate the average annual incidence of ESRD in the 36 ATSIC regions. These population estimates are adjusted for net census undercount and non-response to the Census question about Indigenous status.[13]

From 1st January 1993 to 31st December 1998, 719 Indigenous patients started treatment in Australia. We collected primary data from every hospital's renal unit on the place of usual residence of Indigenous patients prior to their commencing ESRD treatment.[24] We assigned the place of usual residence for Indigenous patients to the appropriate ATSIC regions. We used indirect standardization to calculate an ESRD age and sex standardized incidence ratio with 95% confidence intervals for each ATSIC region for the period 1993–1998. Rates for the total Australian population for the same years were used as the reference.

Measurement of socioeconomic status

Individual level data regarding income, education and employment status are not collected by ANZDATA. We therefore used ATSIC regional level socioeconomic data from the 1996 census. As there is no generally accepted area-based index of socioeconomic disadvantage for Indigenous Australians, we selected five indicators that feature strongly in deprivation indexes used in public health research.[27-29] The specific indicators were:

- proportion of adults who left school aged 15 or less, or who did not attend school,[30]
- unemployment rate,[30]
- median household income divided by average number of persons per household,[31]
- average number of persons per bedroom,[30]
- proportion of births less than 2500 grams.[32]

We generated a summary rank of socioeconomic disadvantage by combining the regional rankings on each socioeconomic indicator with each indicator given equal weight. Data were from the 1996 census or from perinatal statistics collections for 1994–1996. Only people identified as Indigenous Australians are included in the numerators and denominators for these indicators.

In 1996, 22.3% of the Indigenous Australian labour force was estimated to be employed through the Community Development Employment Projects (CDEP) scheme,[33] a 'work for the dole' scheme targeted at Indigenous communities. Employment is often part time, may be seasonal or intermittent[33] and is often compensated at a pay rate equivalent to the unemployment benefit. Although counted as employed in official employment statistics, we have defined CDEP participants as unemployed. This is consistent with the classification of non-Indigenous Australians on 'work for the dole' schemes, who are counted as unemployed in official statistics.

Statistical analysis

Spearman's rank correlation coefficients were calculated to determine the association between the standardized incidence ratios for ESRD and the 36 ATSIC regions' values for each indicator and for the summary rank of disadvantage. Stata 7.0 was used for statistical analysis.

Ethical approval

We obtained ANZDATA approval to analyse geographic data for indigenous patients who began treatment for ESRD in 1993–1998. We also obtained approval for the study from the joint institutional ethics committee of the Royal Darwin Hospital and the Menzies School of Health Research.

3.4: Results

During 1993–1998, the average crude annual incidence of ESRD among Indigenous Australians was 310/1,000,000 persons per year and among the total Australian population was 76/1,000,000 persons per year. After adjusting for age and sex, Indigenous Australians were greater than eight times more likely to develop ESRD compared to the general population of Australia. There was also marked regional variation in the standardized incidence of ESRD among Indigenous Australians (Figure 3.1), with a large gradient from urban to remote regions.

Strong associations are evident between the indicators of socioeconomic disadvantage and the incidence of ESRD (Table 3.1). The correlation with the summary rank of socioeconomic disadvantage is particularly strong (Table 3.1 and Figure 3.2). The wide range shown for each socioeconomic indicator (Table 3.1) attests to the heterogeneity of the Indigenous Australian population with respect to measures relating to social disadvantage, such as access to educational and employment opportunities, housing and living conditions, and birth outcomes.

Indigenous Australians in the regions in the highest quartile of disadvantage have a standardized incidence of ESRD 7.8 times higher (95% CI 6.9–8.8) than that for Indigenous Australians in the regions in the lowest quartile of disadvantage, and 18.5 times higher (95% CI 16.3–20.9) than that for all Australians. If it were possible to reduce the incidence of ESRD amongst all Indigenous Australians to that of Indigenous Australians in the regions in the quartile of least disadvantage, 68% of cases could be avoided. Reduction of the incidence of ESRD among all Indigenous Australians to that of the total Australian population would result in 87% fewer ESRD cases.

3.5: Discussion

This study has demonstrated a striking gradient in the incidence of ESRD among Indigenous Australians that is strongly associated with area-based markers of disadvantage. Importantly however, poor renal health outcomes for Indigenous Australians are not confined to the most disadvantaged or most remote regions, but exist across the entire Indigenous Australian population. The socioeconomic gradient in this study is much steeper than the gradients found in research examining inequalities in health of other total national populations.[3,34,35] A recent study showed that within Australian capital cities, with predominantly non-Indigenous populations, there was a significantly higher incidence of ESRD in more disadvantaged areas.[36] The gradient in incidence was, however, much less steep, with the highest standardised incidence ratio being 1.63 in Fairfield-Liverpool, a disadvantaged area of Sydney. A whole array of socioeconomic, environmental, cultural and political factors affects the health of Indigenous Australians, and both absolute poverty and relative disadvantage are relevant to the steep gradient demonstrated here.

Few previous studies have examined the association between socioeconomic disadvantage and the incidence of ESRD. Khan et al.[37] found no difference in socioeconomic status between patients commencing ESRD treatment and the general population in the Grampian region of Scotland. Byrne et al.[38] examined the incidence of ESRD in New York State using an area-based index of socioeconomic status derived from income, occupational and educational data. They found a relationship between socioeconomic status and ESRD in Whites, but not in Blacks. Young et al.[39] examined the relationship, by county of residence, between the incidence of ESRD and average per capita income for the entire United States. They found similar gradients of risk across income categories for Blacks and Whites: approximately 60% higher incidence in the lowest compared to the highest income category. Perneger et al.,[40] in a population based case-control study of patients commencing ESRD treatment in Maryland, Virginia, West Virginia and Washington, DC, found that the adjusted risk for the development of

ESRD was 4.5 times higher in the lowest compared to the highest income category. They found similar gradients across the Black and White populations.

There are a number of potential sources of bias in our study. First, the propensity to identify as an Indigenous Australian might differ between regions. ANZDATA relies upon self-identification, as does the Australian Bureau of Statistics in its census collections. We believe that the quality of identification in this study is high. Complex management issues require frequent contact between ESRD patients and their medical and nursing staff. Renal staff are very much aware of the high incidence of ESRD among Indigenous Australians. The most likely error would be the failure to identify some urban Indigenous Australian ESRD patients; however, the same potential for error exists for the census data collection. This could result in an imprecise estimate of the true incidence of ESRD amongst Indigenous Australians in urban areas. However, the observed gradient in ESRD incidence is so large that it is unlikely to be significantly altered by problems of identification.

Second, ESRD incidence is calculated using ANZDATA Registry data. If there were significant numbers of Indigenous Australians not being referred for treatment, most probably in remote areas, the true incidence of ESRD would be higher than that observed in those regions. This would further increase the gradient in incidence of ESRD. Differential rates of acceptance of Indigenous Australian patients onto dialysis would potentially bias results. However, Australian guidelines regarding acceptance onto dialysis,[41] which reflect a consensus view among nephrologists, stress equal rights of access to treatment, regardless of race. There is also no evidence that renal units in particular regions provide incomplete reports of the numbers of patients commencing ESRD treatment.

Third, we have used area-based indicators of socioeconomic status, which measure the average level of disadvantage of all persons in that area who

identify as Indigenous Australians, to infer an association between disadvantage and the incidence of ESRD. It is plausible that ecological or community level exposures directly affect health outcomes in this setting. Indigenous Australians in disadvantaged communities may have poor access to preventive health services, no access to stores selling healthy foods at reasonable prices, and inadequate community infrastructure for basic water, sewerage and housing needs. There may however, be other individual, area or population level factors not measured in this study which explain the association we have observed.

Fourth, we have described an association between current disadvantage and the incidence of ESRD. The time interval between exposures and the development of ESRD varies, but typically renal disease progresses over at least several years. Therefore, the most relevant etiological data would be socioeconomic data from an earlier period. However, due to limitations in data availability and quality, we cannot reliably assess trends in levels of Indigenous disadvantage over time.[23]

Nephrologists view renal disease from a biomedical perspective, in which primary disease processes cause ESRD and social determinants of disease are largely irrelevant. A limited biomedical perspective cannot explain the striking gradient in the incidence of ESRD in Indigenous Australians, or the strong association with socioeconomic disadvantage. We propose a broader understanding of the etiology of ESRD in Indigenous Australians that encompasses social, environmental and cultural determinants of health. We believe that multiple etiological factors throughout life,[42] possibly including a genetic predisposition, congenital factors, and childhood and adult influences, determine the patterns of incidence of ESRD. Biomedical interventions alone, using pharmacological and lifestyle interventions for high-risk groups, are not likely to be sufficient to eliminate the excess burden of renal disease in Indigenous Australians.

In recent years there have been efforts to address social disadvantage in Indigenous communities. However, the disadvantages faced by Indigenous Australians are significant and long-standing, and have so far proven difficult to tackle successfully. Large-scale infrastructure development has occurred in a number of Indigenous communities, with projects including ensuring adequate water supply, sanitation, housing and drainage.[43] However, a recent survey of 3609 (79%) houses funded by the Indigenous Housing Authority of the Northern Territory showed that 62% of houses did not meet standards required for the storage and preparation of food, and in 45% of houses, facilities in which to bathe and for the safe removal of human waste were not functional.[43] A recent review of Indigenous education strategies revealed deteriorating outcomes, with an overall decline in school attendance, low rates of retention to the end of high school, and very low proportions of Indigenous compared to non-Indigenous students achieving national reading benchmarks in primary school.[44] The CDEP scheme, an Indigenous community-based employment and community development initiative, was established in 1977 with a major objective being to improve the employment and income status of Indigenous people[45]. Despite a review that recommended reforms to provide participants with a conduit to mainstream employment[46] and subsequent reorientation of the CDEP program to emphasise employment and training,[47] only 13% of participants leaving CDEP in 1999-2000 moved into mainstream employment, education or training positions.[47]

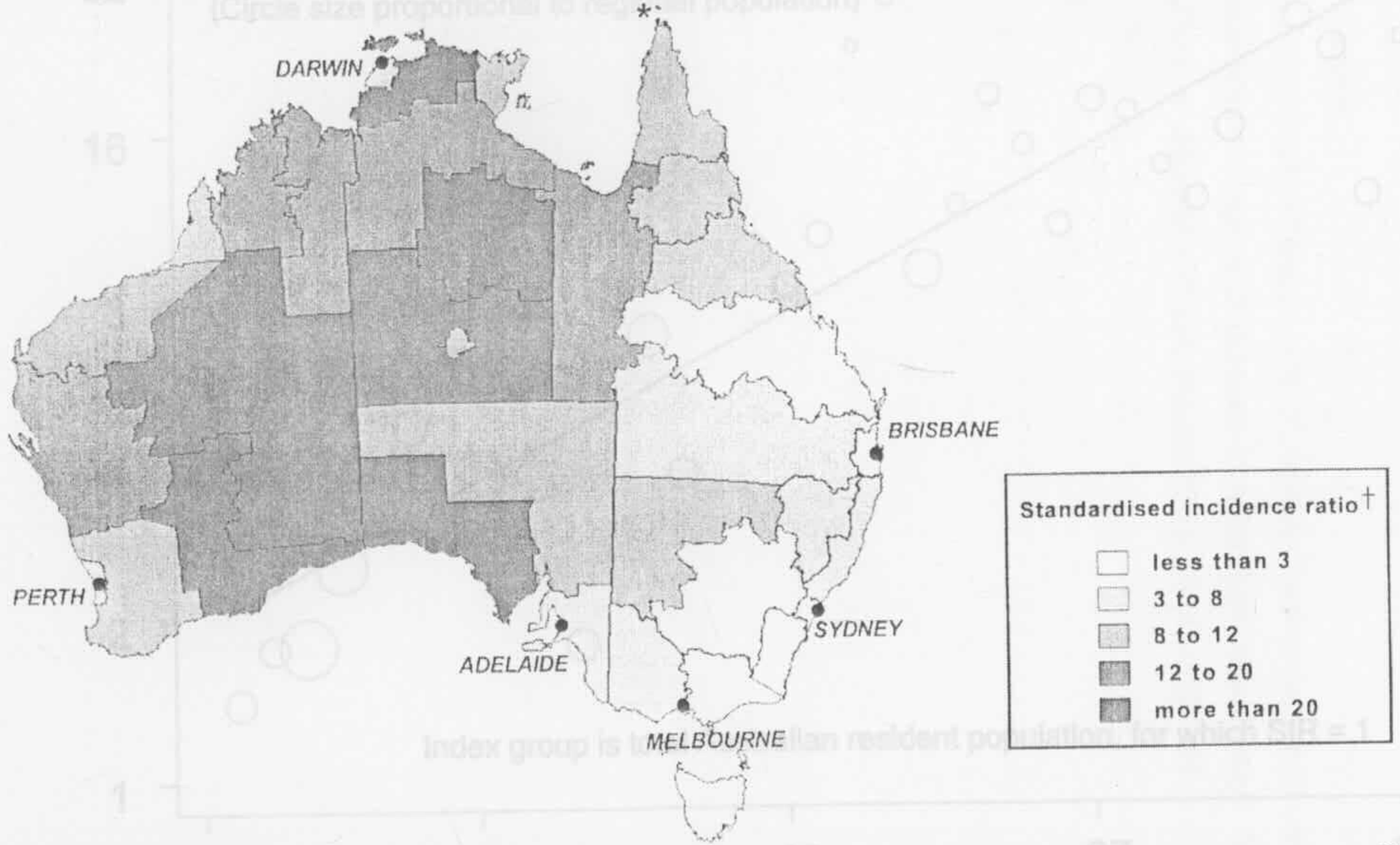
One explanation for the lack of success in reducing disadvantage is that Indigenous people have not always had a significant role in the leadership, planning and delivery of these services.[48] Indigenous Australians must be full and active partners in the development of appropriate interventions to address the profound socioeconomic disadvantages and resultant health inequalities. Such partnerships are required not only to reduce the burden of renal failure and related chronic diseases, including diabetes and cardiovascular disease, but also as a matter of social justice.

Table 3.1: **Correlation between indicators of socioeconomic disadvantage and standardised incidence of ESRD for Indigenous Australians at ATSIC regional level**

Socioeconomic Indicator (units)	Range	Correlation Coefficient*	P value
Early school leavers (%)	12.5 - 52.4	0.68	<0.001
Unemployment rate (%)	20.2 - 74.8	0.72	<0.001
Household income ($ AUS per household member per week)	$80 - 194	- 0.71	<0.001
House crowding (persons per bedroom)	1.1 - 3.2	0.84	<0.001
Low birthweight (%)	7.6 - 21.6	0.49	0.003
Summary rank of disadvantage	1 - 36	0.88	<0.001

*Spearman's rank correlation coefficients.

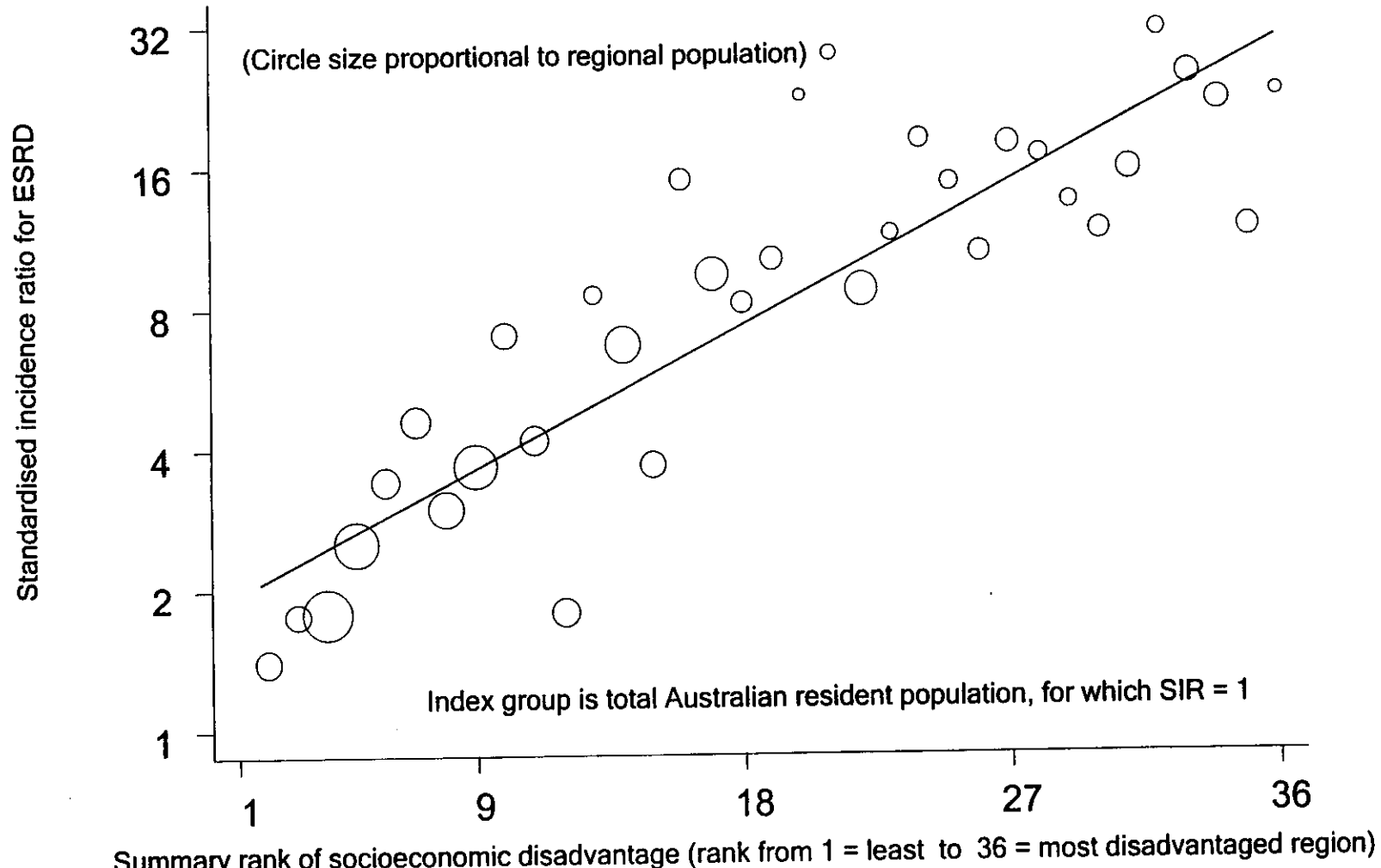
Figure 3.1: **Standardised incidence of ESRD in the Indigenous population by ATSIC region**



* The standardised incidence ratio for the Torres Strait ATSIC region was 15.0. The region is too small to represent at this level of map resolution.

† The index population for standardisation was the total Australian resident population.

Figure 3.2: Socioeconomic Disadvantage and Indigenous ESRD Incidence by ATSIC region



CHAPTER 4: SOCIAL DISADVANTAGE AND VARIATION IN THE INCIDENCE OF END-STAGE RENAL DISEASE IN AUSTRALIAN CAPITAL CITIES

Publication details:

Cass A, Cunningham J, Wang Z, Hoy W. Social disadvantage and variation in the incidence of end-stage renal disease in Australian capital cities. *Australia and New Zealand Journal of Public Health* 2001; 25 (4): 322-326.

4.1: Abstract

Objective: To evaluate variation in the incidence of end-stage renal disease (ESRD) within Australian capital cities. To explore the relation between the incidence of ESRD and socioeconomic disadvantage.

Methods: We obtained data from the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA) regarding 5013 patients from capital cities who started ESRD treatment between 1 April 1993 and 31 December 1998. We used the postcode at the start of treatment to calculate the average annual incidence of ESRD for each of 51 capital city regions using 1996 Census counts based on place of usual residence. We calculated standardised incidence ratios with 95% confidence intervals for each region. The standardised incidence ratios were examined in relation to the SEIFA Index of Relative Socio-Economic Disadvantage (IRSD), derived from the 1996 Census. Low IRSD values indicate more disadvantaged areas.

Results: There is significant variation in the standardised incidence of ESRD within capital cities. There was a significant correlation ($r = -0.41$, $p = 0.003$) between the standardised incidence ratio for ESRD and the SEIFA IRSD.

Conclusions and Implications: Capital city areas that are more disadvantaged have a higher incidence of ESRD. Socio-economic factors may be important determinants of the risk of developing ESRD.

4.2: Introduction

Geographical differentials in morbidity and mortality have been demonstrated in Australian research.[1,3,4,49] These differences have been attributed to socio-economic status,[1,3-5,35] access to health services,[2,6,7] ethnicity[4] and racial discrimination.[8] There has been no previous report of variation in total ESRD incidence at a geographical level below that of State or Territory. A majority of the Australian population live in capital cities (63.1%), and in this study we have evaluated variation in incidence of ESRD within capital cities and the relation between the incidence of ESRD and social disadvantage.

4.3: Methods

Databases

The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) maintains a database of patients treated by maintenance dialysis or renal transplantation in Australia.[25] The registry is funded by the Australian Federal and State governments, the New Zealand government and the Australian Kidney Foundation. All renal units that provide ESRD treatment in Australia participate in the Registry. Survey forms are completed six monthly for all patients until (and including) the date of death. The only patients not registered are the few who die before being established on a maintenance dialysis or transplant program.[26] Postcode of residence at the start of treatment has been collected for all new patients entered into the ANZDATA Registry since 1 April 1993.

Data validity

Postcode of residence at the start of treatment is an imperfect indicator of the usual place of residence before starting treatment. We restricted this analysis to Australian capital cities, in part due to concern regarding the validity of postcode data for patients from remote areas. Renal units that provide dialysis and transplant services are concentrated within capital cities, and patients do not need to relocate within capital cities in order to access services.

Patients

From 1 April 1993 to the 31 December 1998, 8,158 patients started treatment. We excluded 50 patients (0.6%) from analysis because treatment was commenced overseas or the patient was an overseas visitor. We excluded a further 3 patients (0.04%) because no postcode data was available. 3,092 patients had postcodes from non-capital city areas. In total, 5,013 patients were included in the study.

Geography

We used Statistical Sub Divisions (SSDs) as our geographical units for analysis. SSDs are areas defined in the Australian Standard Geographical Classification[50] and are used by the Australian Bureau of Statistics (ABS) as geographical units for analysis. They aggregate to form Statistical Divisions (SDs), which aggregate to form States and Territories. Capital cities contain several SSDs except Hobart, which is a single SSD. We assigned postcodes at entry to SSDs using concordances provided by the ABS. We also aggregated SSDs within Darwin and Canberra to form single geographical areas due to the small population size of SSDs within these capital cities. Seven hundred and ninety-nine patients (15.9%) had postcodes that crossed capital city SSD boundaries. These patients were allocated to regions based on the proportion of the population within each postcode that fall within the respective SSDs (ABS unpublished data).

Measurement of socio-economic status

The ABS has developed indexes to describe the socio-economic characteristics of an area. This study uses the Index of Relative Socio-Economic Disadvantage (IRSD). The IRSD is constructed using principal component analysis and is derived from attributes such as low income, low educational attainment, high unemployment and jobs in relatively unskilled occupations.[51] The higher an area's index value, the less disadvantaged that area is compared to other areas. The index scores are standardised so that the national mean score is 1000.

Statistical analysis

We used 'place of usual residence' counts from the 1996 Census (ABS unpublished data) as population denominators. We used indirect standardisation to calculate an age and sex standardised incidence ratio (SIR) with 95% confidence intervals for each region. Rates for the total Australian resident population were used as the reference. Pearson correlation coefficients were calculated to determine the association between the IRSD

values for the 51 regions and the SIRs for ESRD. This analysis was weighted according to the size of the regional population. We estimated the percentage of cases of ESRD in the relatively disadvantaged capital city areas (IRSD < 1000) that could be avoided if these areas had the same adjusted incidence rate as the relatively advantaged capital city areas (IRSD > 1000). Statistical analysis was performed using Stata (Release 7.0, College Station, Texas, 2000).

Ethical approval

We obtained ANZDATA approval to analyse geographic data for patients starting treatment for ESRD between 1 April 1993 and 31 December 1998. We also obtained approval for the study from the joint institutional ethics committee of Royal Darwin Hospital and the Menzies School of Health Research.

4.4: Results

The standardised incidence ratio for ESRD within capital cities varied significantly from 0.37 to 3.23 (Table 4.1). There was marked variation within most capital cities. Mapping the standardised incidence of ESRD reveals that significant geographic sectors of capital cities have an excess of ESRD in population terms. These are generally the sectors which include relatively disadvantaged SSDs.

In Sydney, the inner west and south-western sectors have the highest incidence (Figure 4.1). In Melbourne, Greater Dandenong City, the inner city and north-western sectors have the highest incidence of ESRD (Figure 4.2). All the regions in Brisbane had average to below average standardised incidence of ESRD (Figure 4.3 and Table 4.1). Brisbane City SSD, with almost 800,000 residents, had 60% of new cases in the total Brisbane area. There were few cases of ESRD in the areas with small resident populations; Gold Coast City Part A, Beaudesert Shire Part A and Redcliffe City (Table 4.1). The corresponding 95% confidence intervals for the SIRs for these areas are broad. In Adelaide, the west has high incidence and the east low incidence (Figure 4.4 and Table 4.1). In Perth, the south-eastern area has the highest incidence of ESRD (Figure 4.5). Residents of Canberra (SIR 0.89) and Hobart (SIR 0.90) had close to average standardised incidence of ESRD. Darwin had the highest standardised incidence (SIR 3.23) (Table 4.1).

There was a significant correlation ($r = -0.41$, $p = 0.003$) between the standardised incidence ratio for ESRD and the IRSD (Figure 4.6), which indicates a higher incidence of ESRD with greater disadvantage (lower IRSD scores). This analysis was weighted according to the size of the regional population. The Darwin region is a significant outlier, due to a much higher Indigenous proportion in the urban population (9.5%) and much higher Indigenous proportion of ESRD cases (63.5%). This region was excluded from the graphical representation of the relationship between disadvantage and the incidence of ESRD (Figure 4.6), but included in the correlation. If the relatively disadvantaged capital city areas (IRSD < 1000) had the same adjusted

incidence rate of ESRD as the relatively advantaged capital city areas (IRSD > 1000), 22.8% of cases, or 463 cases in this almost six-year period, would be avoided.

4.5: Discussion

This study demonstrates that there is significant variation in the standardised incidence of ESRD within Australian capital cities. The variation is evident in each capital city where population size allows analysis at a smaller geographical level. The division of Brisbane into SSDs of very unequal population size impairs the ability to examine for variation in ESRD incidence. Within the Brisbane City SSD, of almost 800,000 resident population, there is a very wide range in the IRSD score at Collection District (CD) level, from a minimum of 548 to a maximum of 1201. This indicates that Brisbane City SSD contains areas of both major disadvantage and advantage that are concealed due to the population and geographic size of the SSD. Analysis at the sub-SSD level within Brisbane City might be more appropriate to address the issue of geographical variation in incidence of ESRD.

The results of this study also indicate that variations in relative disadvantage are significantly associated with the standardised incidence of ESRD. The analysis includes all capital cities, not a selected subset. It is generally robust as the vast majority of areas have relatively large population size and number of ESRD cases in the study period. This finding is consistent with a body of Australian and international literature regarding the social determinants of health and illness.

There are potential sources of bias in this analysis. The standardised incidence ratios are calculated using data from the ANZDATA Registry concerning number and geographical location of ESRD cases. If certain renal units provide incomplete reports of the number of patients starting treatment, it would bias results. However, all renal units that provide ESRD treatment in Australia participate fully in the Registry.[26] Although there may be anecdotal evidence concerning remote areas, there is no evidence that people with ESRD in capital cities are not referred for dialysis. Differential acceptance onto dialysis would also potentially bias results. The Australian Kidney Foundation and Australia and New Zealand Society of Nephrologists have recently

released draft guidelines regarding caring for people with renal impairment.[41] The guidelines state: "The cardinal factor for acceptance onto dialysis is whether dialysis is likely to be of benefit to the patient. People in our society have equal rights to access public medical facilities (including treatment of ESRD) regardless of age, race, sex, religion and underlying disease". The guidelines relating to acceptance onto dialysis reflect a consensus view from clinical practice and thus differences in acceptance are unlikely to explain variation in incidence within capital cities.

Postcode of residence at the start of treatment may not be a valid indicator of the usual place of residence before starting treatment. If the postcode of a temporary residence at the time of starting treatment was recorded in ANZDATA, rather than the postcode of the usual place of residence, this would potentially bias results. It is unlikely that people would need to relocate within a capital city to access medical services or to commence ESRD treatment. However, people living in remote areas may need to change their residence around the time of starting treatment in order to access renal services.

Although some people included as capital cities cases may have moved from non-capital city areas to access treatment, renal treatment services are increasingly available in large regional centres. Patients are able to commence and stabilise on treatment in regional centres. Indeed, 3092 patients (37.9% of the total cohort) have a non-capital city postcode at entry recorded. There is no evidence that patients who temporarily relocate to capital cities, and are incorrectly coded with the postcode of the temporary place of residence, are more likely to go to an area of low rather than high socioeconomic status. Coding errors relating to temporary relocation to capital cities are unlikely to substantially affect incidence ratios of ESRD in the capital cities.

Research in nephrology has focused on an understanding of renal disease as caused by primary and proximal disease processes. This cannot explain all

the variation in incidence of ESRD found in this study or the striking gradient in ESRD incidence from urban to rural areas found among Indigenous Australians.[24] To explain the significant association between relative disadvantage and the standardised incidence of ESRD observed in this study, we need to develop a framework for understanding the etiology of renal disease that encompasses social and environmental determinants of health. The challenge will be to identify the pathways that connect the upstream social factors with the downstream disease processes that are known to lead to ESRD.

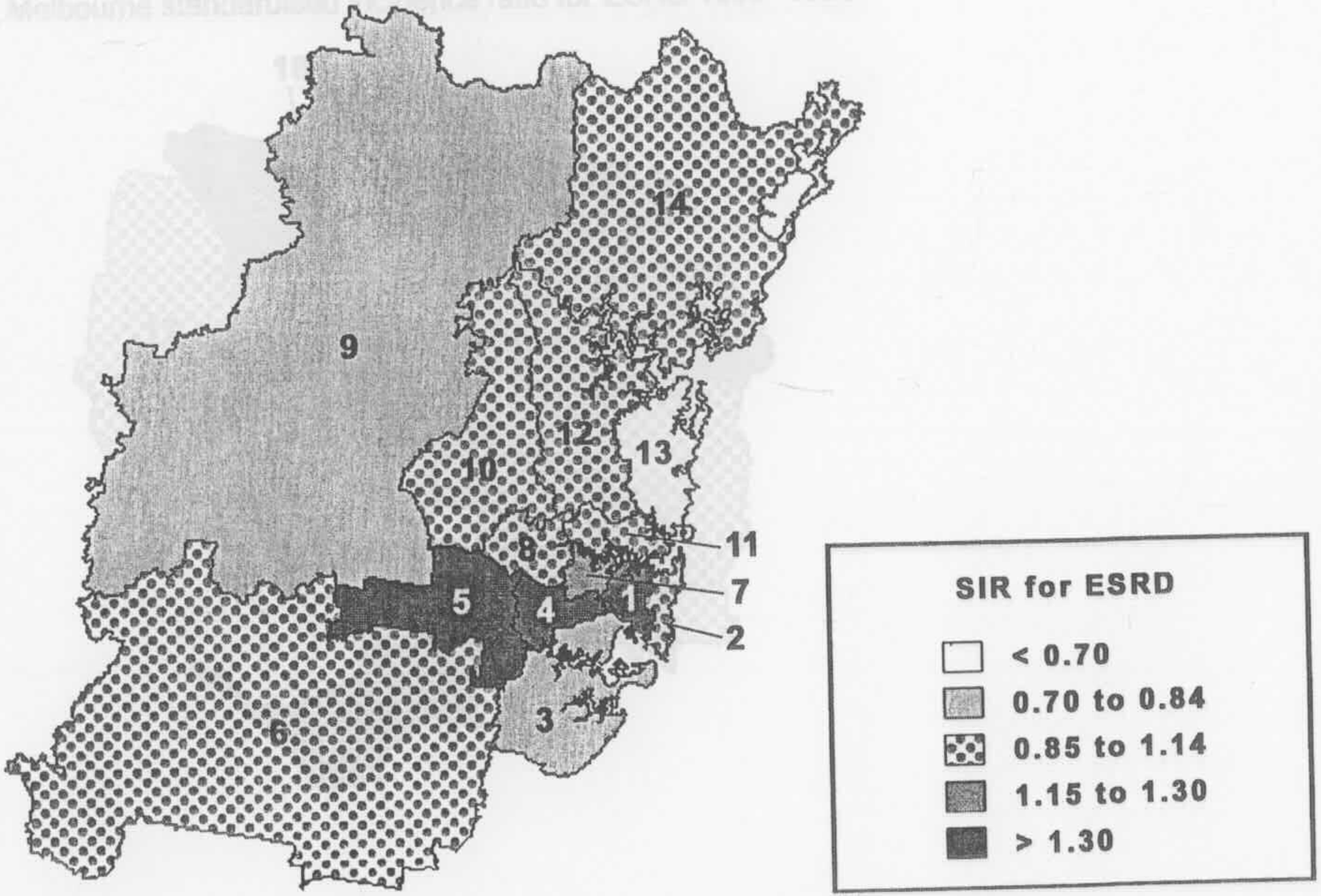
Table 4.1: **Standardised incidence ratio for ESRD in Australian capital cities, 1993–1998.**

City	Area (map references)	Population	Cases	SIR* (95%CI)
Sydney	Inner Sydney (1)	255,499	165	1.41 (1.21–1.65)
	Eastern Suburbs (2)	227,080	109	1.01 (0.83–1.22)
	St George-Sutherland (3)	393,497	142	0.74 (0.63–0.87)
	Canterbury-Bankstown (4)	290,138	188	1.34 (1.16–1.55)
	Fairfield-Liverpool (5)	302,046	197	1.63 (1.41–1.87)
	Outer South Western Sydney (6)	209,973	74	1.01 (0.79–1.26)
	Inner Western Sydney (7)	147,774	85	1.16 (0.93–1.44)
	Central Western Sydney (8)	268,683	137	1.13 (0.95–1.33)
	Outer Western Sydney (9)	293,242	90	0.79 (0.64–0.98)
	Blacktown-Baulkham Hills (10)	352,697	158	1.13 (0.96–1.33)
	Lower Northern Sydney (11)	264,779	123	0.97 (0.81–1.16)
	Hornsby-Ku-ring-gai (12)	236,562	102	0.90 (0.74–1.10)
	Northern Beaches (13)	212,387	68	0.65 (0.50–0.82)
	Gosford-Wyong (14)	263,055	152	1.12 (0.95–1.31)
Melbourne	Inner Melbourne (15)	215,427	120	1.24 (1.03–1.48)
	Western Melbourne (16)	389,408	205	1.16 (1.01–1.33)
	Melton-Wyndham (17)	113,637	34	0.89 (0.61–1.24)
	Moreland City (18)	131,082	83	1.22 (0.97–1.51)
	Northern Middle Melbourne (19)	235,942	137	1.17 (0.99–1.39)
	Hume City (20)	116,441	55	1.29 (0.97–1.68)
	Northern Outer Melbourne (21)	157,779	66	1.12 (0.86–1.42)
	Boroondara City (22)	146,657	42	0.60 (0.43–0.81)
	Eastern Middle Melbourne (23)	396,342	176	0.87 (0.74–1.01)
	Eastern Outer Melbourne (24)	225,159	73	0.79 (0.62–0.99)
	Yarra Ranges Shire Part A (25)	132,303	45	0.84 (0.61–1.12)
	Southern Melbourne (26)	364,925	166	0.90 (0.77–1.04)
	Greater Dandenong City (27)	126,887	79	1.36 (1.08–1.70)
	South Eastern Outer Melbourne (28)	186,260	67	0.98 (0.76–1.25)
	Frankston City (29)	105,728	29	0.62 (0.42–0.89)

	Mornington Peninsula Shire (30)	114,183	60	0.98 (0.75–1.26)
Brisbane	Brisbane City (31)	791,840	326	0.90 (0.80–1.00)
	Gold Coast City Part A (32)	40,462	7	0.44 (0.18–0.90)
	Beaudesert Shire Part A (33)	23,115	3	0.37 (0.08–1.08)
	Caboolture Shire Part A (34)	94,092	28	0.67 (0.44–0.96)
	Ipswich City (35)	114,675	43	0.97 (0.70–1.31)
	Logan City (36)	158,322	52	0.95 (0.71–1.25)
	Pine Rivers Shire (37)	103,517	24	0.65 (0.42–0.97)
	Redcliffe City (38)	48,369	25	0.95 (0.62–1.41)
	Redland Shire (39)	100,135	37	0.85 (0.60–1.17)
Adelaide	Northern (40)	327,224	133	0.93 (0.78–1.10)
	Western (41)	202,917	126	1.15 (0.96–1.37)
	Eastern (42)	211,655	65	0.62 (0.48–0.79)
	Southern (43)	308,391	116	0.78 (0.64–0.94)
Perth	Central Metropolitan (44)	111,680	55	1.05 (0.79–1.36)
	East Metropolitan (45)	205,454	87	1.00 (0.80–1.24)
	North Metropolitan (46)	379,721	159	0.98 (0.83–1.14)
	South West Metropolitan (47)	255,278	86	0.75 (0.60–0.92)
	South East Metropolitan (48)	289,519	146	1.17 (0.99–1.38)
Hobart	Hobart (49)	191,136	79	0.90 (0.71–1.12)
Darwin	Darwin (50)	78,397	85	3.23 (2.58–3.99)
Canberra	Canberra (51)	297,943	104	0.89 (0.73–1.08)

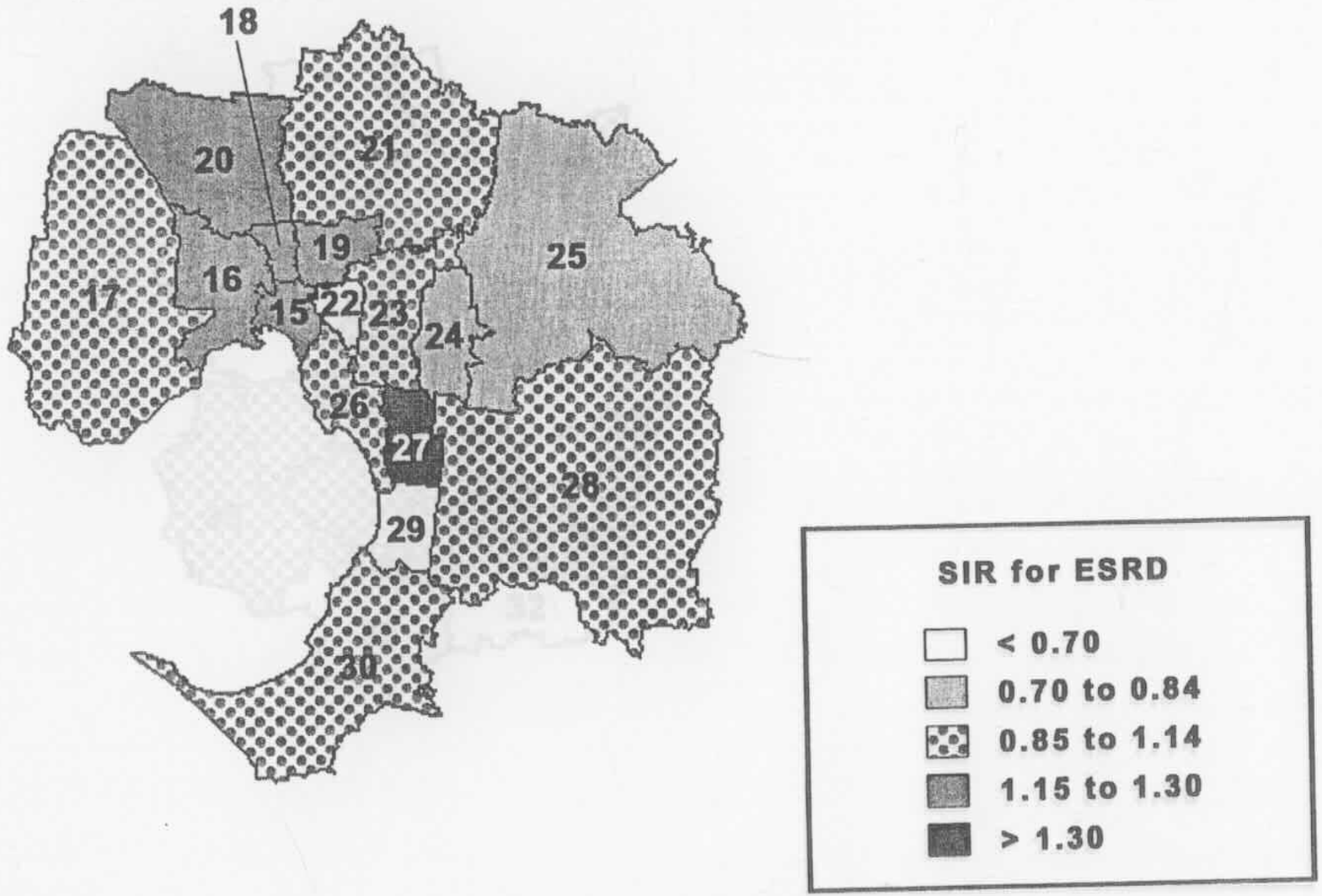
*Indirectly age and sex standardised to the rates for the total Australian resident population. The value for all Australia = 1.00.

Figure 4.1: Sydney standardised incidence ratio for ESRD 1993--1998



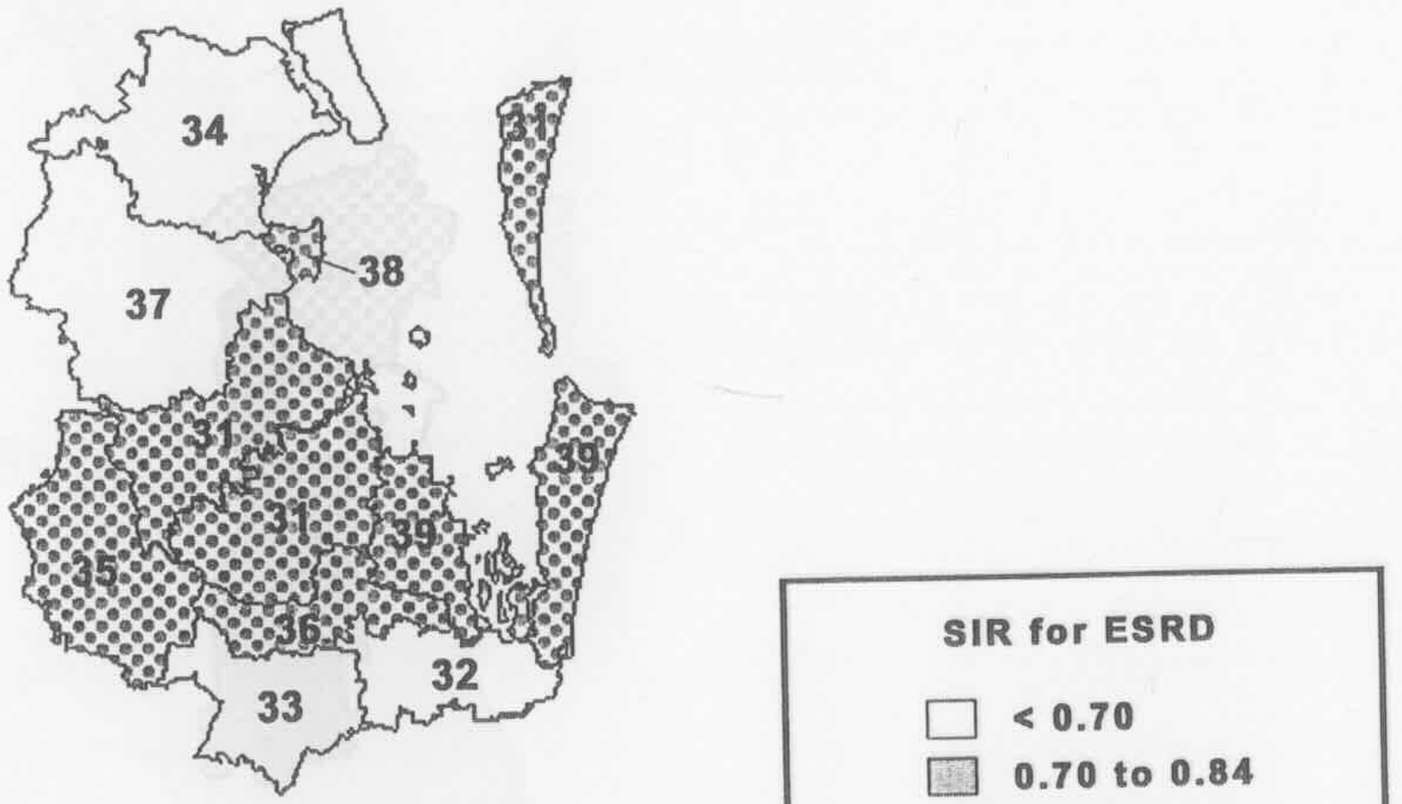
Map numbers refer to capital city areas specified in Table 4.1

Figure 4.2: Melbourne standardised incidence ratio for ESRD 1993--1998



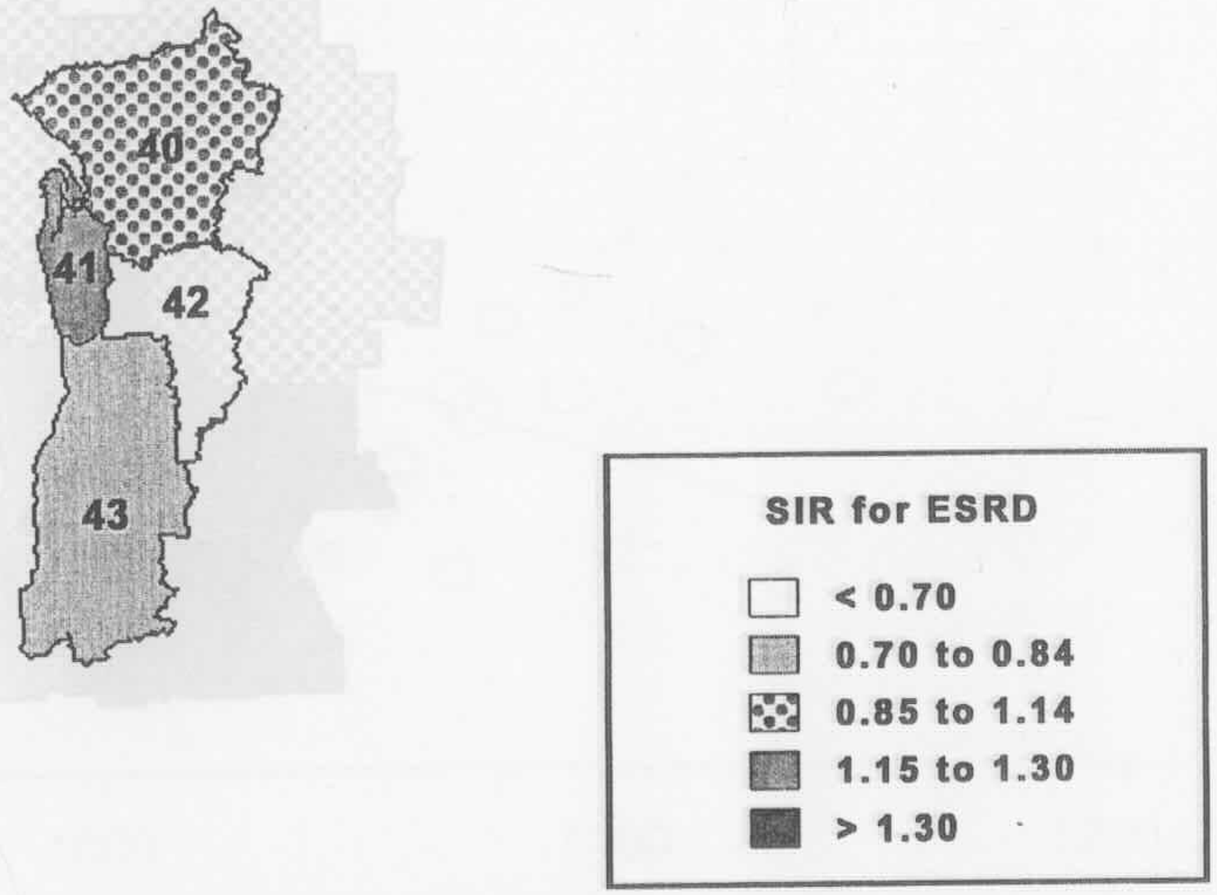
Map numbers refer to capital city areas specified in Table 4.1

Figure 4.3: Brisbane standardised incidence ratio for ESRD 1993--1998



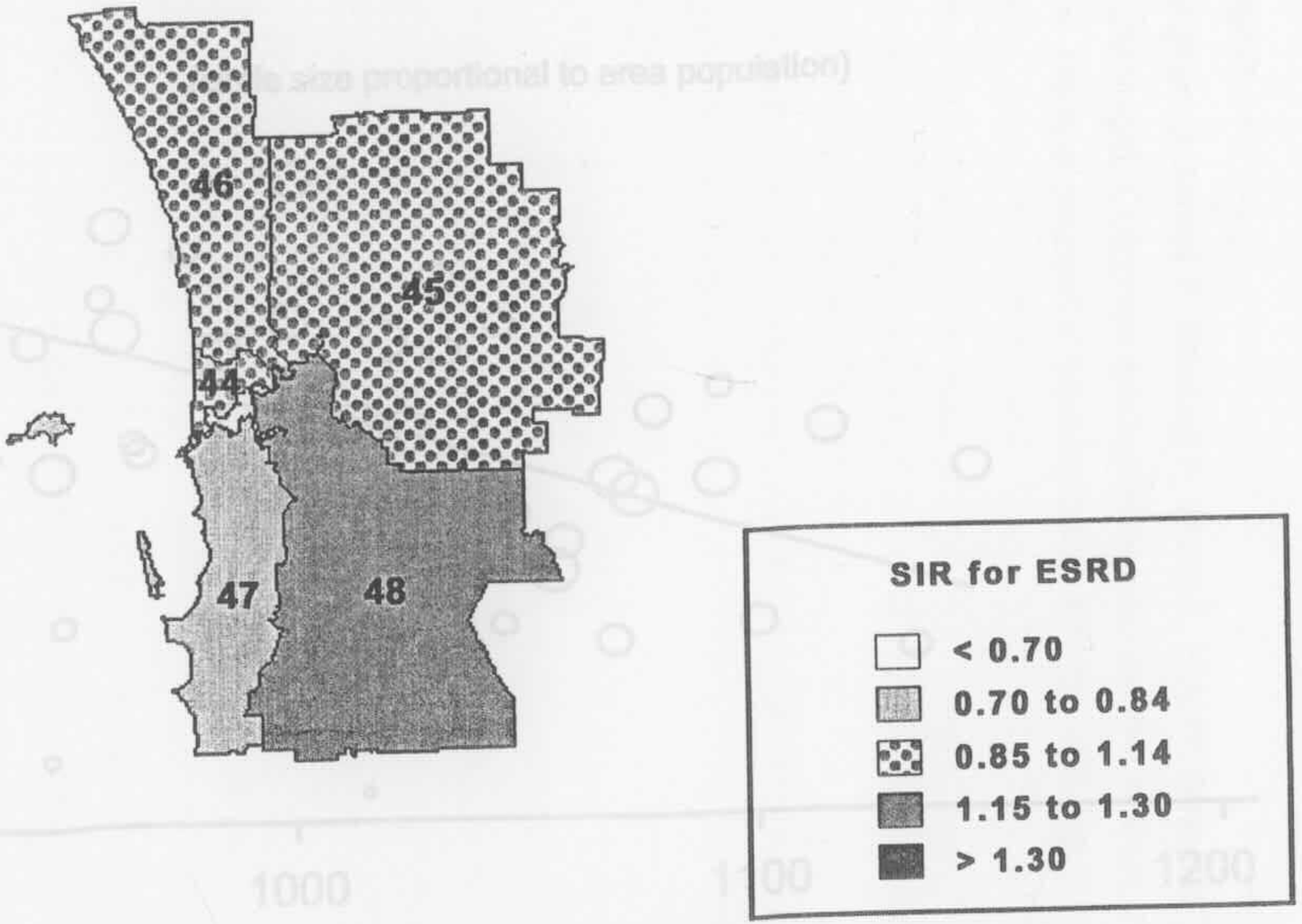
Map numbers refer to capital city areas specified in Table 4.1

Figure 4.4: Adelaide standardised incidence ratio for ESRD 1993–1998



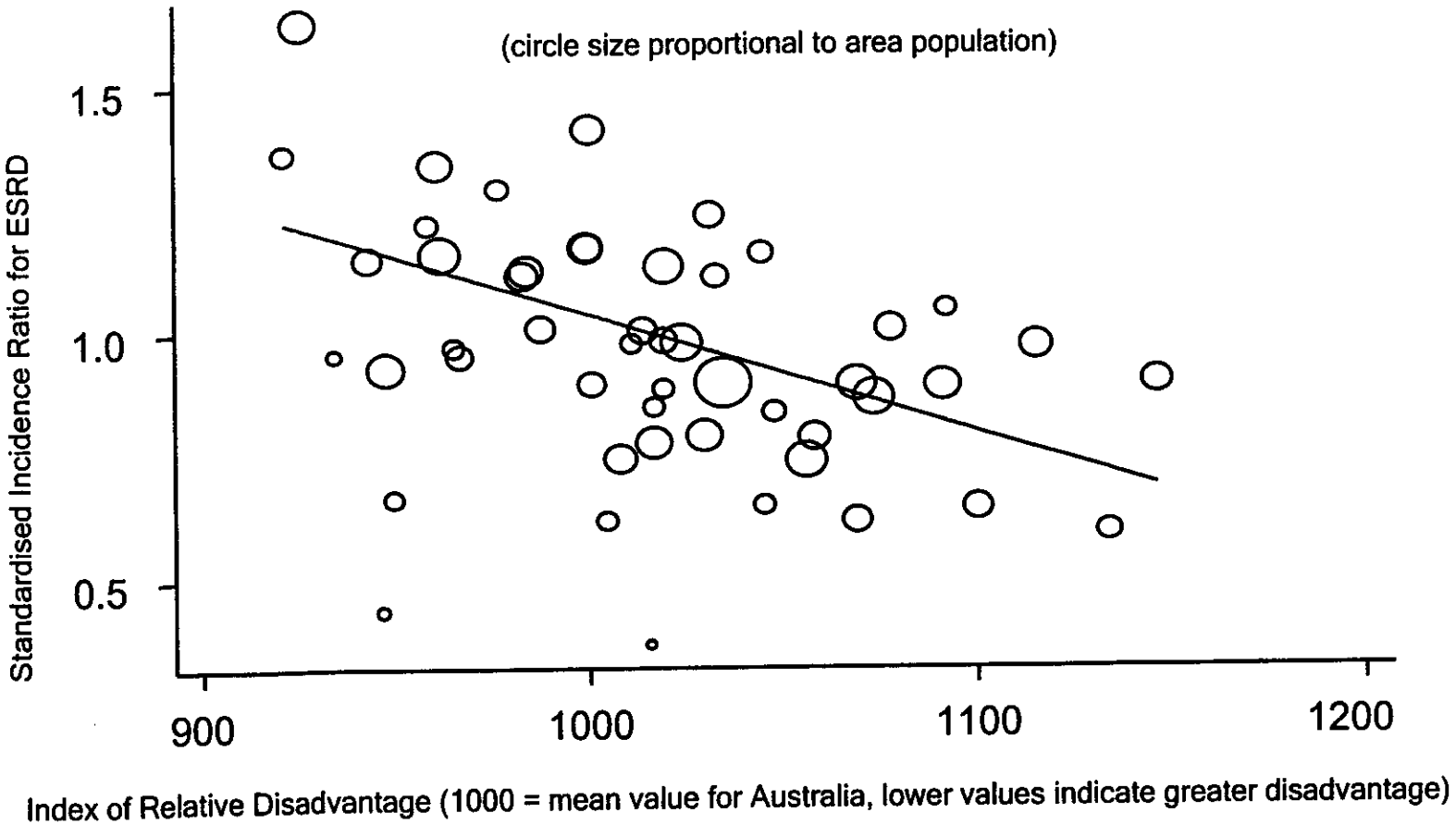
Map numbers refer to capital city areas specified in Table 4.1

Figure 4.5: Perth standardised incidence ratio for ESRD 1993--1998



Map numbers refer to capital city areas specified in Table 4.1

Figure 4.6: Socioeconomic Disadvantage and capital city ESRD Incidence by SSD



CHAPTER 5: DELAYED REFERRAL TO A NEPHROLOGIST: OUTCOMES AMONG PATIENTS WHO SURVIVE AT LEAST ONE YEAR ON DIALYSIS

Publication details:

Cass A, Cunningham J, Arnold P, Snelling P, Wang Z, Hoy W. Delayed referral to a nephrologist: Outcomes among those who survive at least one year on dialysis. *Medical Journal of Australia* 2002; 177 (3): 135-138.

5.1: Abstract

Objective: To investigate whether late referral to a nephrologist of patients with chronic renal insufficiency influences the likelihood of both transplantation and mortality among those who survive at least one year on dialysis.

Design: Retrospective national cohort study, using data from the Australia and New Zealand Dialysis and Transplant Registry.

Participants: All patients, with end-stage renal disease, who started renal replacement treatment in Australia between 1 April 1995 and 31 December 1998, excluding those who received transplants or who died in their first year on dialysis. Patients referred 'late' were defined as those who needed to commence dialysis within three months of referral to a nephrologist.

Main outcome measures: Length of patient survival, and whether patients received a transplant at any time between one year after starting dialysis and completion of the study on 31 March 2000.

Results: Of the 4,243 patients included in the study, 1,141 (26.9%) were referred late. Late referral (LR) patients were significantly less likely to receive a transplant in their second and subsequent years on dialysis (adjusted rate ratio 0.78, 95% CI 0.64–0.95). LR patients were at significantly increased risk of death after their first year on dialysis (adjusted hazard ratio 1.19, 95% CI 1.04–1.35).

Conclusions: Late referral is associated with increased mortality, even among those who survive their first year on dialysis. Improving the quality of pre-dialysis care might improve access to transplantation and long-term survival. General practitioners could minimise late referrals through targeted screening of high-risk individuals.

5.2: Introduction

The national renal registries of Australia/New Zealand, USA, Canada and Japan have reported an increasing incidence of end-stage renal disease (ESRD) of between 3-8% per annum between 1993 and 1997.[52] Despite improvements in treatment, the mortality of people on dialysis remains high.[53] Annual mortality rates in the various renal registries range from 10 to 20%.[54]

The proportion of ESRD patients referred 'late' to a nephrologist (i.e. patients needing to commence dialysis within 3-4 months of referral) varies widely. In developing countries, the proportion reaches 62%,[55] while in developed countries, it is normally 25-40%.[56-59] Previous US and UK reports have shown that increasing age and co-existing illnesses,[60] ethnicity[61] and membership of a health maintenance organisation[56] are associated with late referral.

Late referral (LR) patients on dialysis experience greater early morbidity and higher early mortality. Late referral, associated with advanced uraemic symptoms, metabolic acidosis, hypertension, pulmonary oedema and pericarditis, frequently results in emergency haemodialysis using central venous catheters.[57-59] It is also associated with longer[57,58] and more costly[57] initial hospitalisation. Early mortality, during the initial 6 to 12 months on dialysis, is higher for LR patients,[55,62] but little is known about survival differences beyond the first year.

This study investigated whether or not late referral to a nephrologist influences the rates of transplantation and mortality among patients who have survived at least one year's dialysis.

5.3: Methods

ANZDATA database

The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) maintains a data- base of patients treated by maintenance dialysis or renal transplantation in Australia.[25] All Australian renal units treating ESRD supply data to the Registry. Survey forms are completed six-monthly for all patients up to and including date of death. The only patients not registered are the few who die before being established on a maintenance dialysis or transplant program. Data on the timing of referral (i.e. whether 'late' or 'not late') have been collected for new patients entered onto the Registry since 1 April 1995.

Data collected

Between 1 April 1995 and 31 March 2000, we followed-up patients with ESRD to examine the long-term effects of late referral on both the likelihood of transplantation and on mortality.

Using the ANZDATA database, we recorded, for each patient, the timing of referral, age, sex, primary renal disease, the presence of selected comorbidities recorded at entry to the program, whether or not the patient was of Indigenous origin and treatment modality (haemodialysis, peritoneal dialysis or transplantation).

LR patients were defined as those needing to commence dialysis within three months of referral to a nephrologist. This definition, consistent with international nephrology research,[58,59,63] reflects the minimum time required to educate patients regarding treatment options and to establish permanent vascular access for haemodialysis.

Comorbid illnesses noted were diabetes, ischaemic heart disease, cerebrovascular disease, peripheral vascular disease and chronic lung disease. Outcomes were patient survival and whether or not the patient

received a transplant at any time between one year after starting dialysis and the completion of the study.

Patients

During the study period, 5,590 patients with ESRD commenced renal replacement therapy (RRT). Excluded from the analysis were 36 patients (0.6%) who had started treatment outside Australia or who were overseas visitors, and 194 patients (3.5%) with ESRD due to rapidly progressive glomerulonephritis, Goodpasture's syndrome, cholesterol emboli, haemolytic uraemic syndrome or cortical necrosis. (As these conditions generally have a very short course from inception to ESRD, contact with renal services earlier than three months before commencing RRT would not usually have been possible.)

In their first year on RRT, fewer LR patients received a transplant (LR 5.5% v non-LR 10.6%; $p < 0.001$) and more died (LR 15.9% v non-LR 9.4%; $p < 0.001$). In order to discount the short-term hazards of an unplanned commencement of dialysis, we focused on patients who survived their first year on dialysis. We therefore excluded 494 patients (8.8%) who received transplants, 600 patients (10.7%) who died and 23 patients (0.4%) who were lost to follow-up within the first year. Our analysis was based on data for the remaining 4,243 patients.

Within the study period, patients were followed up to the time of transplantation, loss to follow-up, or death. Transplantation was chosen as an endpoint for follow-up, as it greatly reduces mortality[9] and would therefore distort the effects of other factors, including late referral.

Statistical analysis

Statistical analysis was performed using Stata (Release 7.0, College Station, Texas, 2000). Using the Cox proportional hazards model, we calculated a rate ratio for transplantation and a hazard ratio for death. Patient survival was

estimated by the Kaplan-Meier method, with the log rank test used to compare survival curves. The first year on dialysis was not included in survival time, as patients had to survive at least that period to be included.

Ethical approval

Our study was approved by the Joint Institutional Ethics Committee of the Royal Darwin Hospital and the Menzies School of Health Research. We obtained the approval of ANZDATA to analyse data for new patients starting RRT between 1 April 1995 and 31 December 1998.

5.4: Results

Of the 4,243 patients included in the study, 1,141 (26.9%) were LR patients (Table 5.1). Hypertensive renal disease, other types of primary renal disease and uncertain diagnoses were more common in the LR group. Primary glomerulonephritis, polycystic disease, analgesic nephropathy and reflux nephropathy were more common in the non-LR group. The LR group had a greater burden of co-morbid illness.

There were no significant differences in age or sex between LR and non-LR patients, but a significantly higher proportion of the LR group were of Indigenous origin (13.4% v 7.7%, $P < 0.001$).

LR patients were less likely to receive a transplant in their second and subsequent years on RRT (unadjusted rate ratio 0.71, 95% CI 0.58–0.86). This difference remained significant after adjustment for age, sex, number of comorbidities, primary cause of renal disease and Indigenous status (adjusted rate ratio 0.78, 95% CI 0.63–0.95).

Kaplan-Meier survival curves, according to timing of referral, showed a significant difference in survival *after* the first year on RRT (P value for log rank test < 0.001) (Figure 5.1). The mortality rate was 20 deaths (95% CI, 18–22) per 100 patient-years for the LR group and 15 deaths (95% CI, 14–16) for the non-LR group. The unadjusted hazard ratio for death in the LR group compared with the non-LR group was 1.30 (95% CI, 1.14–1.48). After adjusting for known predictors of mortality (age, sex, number of co-morbidities, primary renal disease and Indigenous status), the hazard ratio for death in the LR group was still significant (1.19; 95% CI, 1.04–1.35). The hazard ratio for death was significant even when Indigenous patients were excluded from the analysis. Inclusion of a variable that described the dialysis modality in the first year of treatment made no significant difference.

5.5: Discussion

Our results show unequivocally that late referral is associated with increased mortality beyond the initial year of RRT. The association persists even after adjusting for known predictors of mortality, suggesting that additional factors may be involved. A plausible explanation is that late referral may be a reflection of suboptimal pre-ESRD care, affecting patient survival before commencement of dialysis and for years afterwards.

It is possible that the difference in survival rate between LR and non-LR patients is related to the level of renal function at the start of dialysis, which has been shown to be a determinant of patient survival.[64] If non-LR patients start treatment earlier in the course of their chronic renal disease (at a stage when renal function is significantly less impaired), subsequent survival on dialysis may be longer. ANZDATA has, since 1998, collected data regarding the level of renal function at the start of dialysis. Of patients starting RRT during 1998, the LR patients (n = 358) had a mean creatinine clearance of 8.0 mL/min (SD, ± 7.1) and non-LR patients (n = 1133) had a mean clearance of 7.9 mL/min (SD, ± 3.6), a non-significant difference.[9] Assuming that the results would have been similar for the other study years (1995-1997), the observed survival difference would not appear to be directly related to the level of renal function at the start of dialysis.

Incomplete adjustment for intervening and confounding variables may be part of the explanation for the survival difference attributed to late referral. Chandna et al[62] have shown that a total comorbidity severity score is a better predictor of mortality on RRT than the number of comorbidities. We were unable to explore this possibility, as ANZDATA does not collect data on the severity of comorbid illnesses. However, if late referral is an indicator of suboptimal pre-ESRD care, it is plausible that worse outcomes might be due to inadequate management of comorbid illnesses, including vascular disease and heart failure.

Two previous studies[58,59] of the effect of late referral on long-term survival (at least 5 years follow-up) found no significant difference in long-term survival between LR and non-LR patients. Another study[62] found that unplanned presentation (which is not the same as late referral) adversely affected survival. However, all three studies involved fewer than 300 patients and had limited power to detect a significant difference between LR and non-LR groups. By contrast, our study, based on a national cohort, has much greater power. Moreover, because our study (unlike previous studies) excluded all patients who died in their first year on dialysis, we were able to separate the short-term effects of unplanned commencement of RRT from the long-term disadvantage arising from suboptimally managed chronic renal insufficiency.

Our results suggest that improving the quality of pre-ESRD care, through timely referral, might improve long-term survival on RRT. Angiotensin-converting enzyme inhibitors,[65,66], angiotensin-II receptor antagonists[67] rigorous blood pressure control[68] and rigorous glycaemic control[69] have all been proven effective in slowing the progression of chronic renal insufficiency. However, there have been no definitive studies demonstrating methods to reduce mortality in people with chronic renal impairment.

The continuing high incidence of late referral seems to indicate that nephrologists are failing to communicate to physicians and general practitioners the importance of optimal pre-ESRD care. Primary care doctors may be unaware of the severity of renal insufficiency in some patients, particularly if serum creatinine level is the only measure used to monitor renal function.[70] Late referral may stem from uncertainty about the appropriateness of RRT for a given patient[70] or the perception that treatment services are not easily accessible to the patient. In a US survey of general practitioners who referred new ESRD patients to a renal unit, Campbell et al[71] found that key factors delaying referral were lack of knowledge of guidelines (relating to timing and indications for referral) and inadequate communication between nephrologists and general practitioners.

Levin[63] contends "many specialists (and general practitioners) perceive nephrologists only as providers of dialysis therapy ... (and fail to appreciate) the utility of nephrological care during early stages of renal insufficiency". Although the Australian Kidney Foundation has issued guidelines for the care of people with renal impairment,[72] to our knowledge no attempt has been made to assess the awareness of these guidelines among general practitioners and non-nephrologists.

The AusDiab study[73] found that 2.5% of Australian adults aged 25 years and over had significant proteinuria and that 1.1% had a serum creatinine level of over 120μmol/L. This suggests that several hundred thousand Australians have indicators of renal disease. Screening studies in Japan indicate that people with proteinuria are 15 times more likely than those without proteinuria to develop renal failure within ten years.[74] We believe that there is sufficient evidence that progression of chronic renal insufficiency to ESRD can be prevented to suggest that targeted screening for renal disease among people in high-risk groups should be undertaken in general practice. The most important potential benefit, despite the absence of strong evidence, could be reduced mortality among people with chronic renal insufficiency.

We suggest that general practitioners use dipstick urinalysis for proteinuria to screen patients who have any one of the following risk factors: age over fifty, hypertension, diabetes, smoking, family history of renal disease, or being of Indigenous origin. Serum creatinine level should be measured to calculate the glomerular filtration rate using the Cockcroft-Gault equation.[75] Where appropriate, patients should be aggressively treated for hypertension, proteinuria and other vascular risk factors, and if the glomerular filtration rate falls below 30mls/min, referred promptly to a nephrologist.[72]

We must urgently address the lack of a strong evidence base in the management of patients with chronic renal insufficiency. These patients need a continuum of care from the time of diagnosis to the onset of ESRD.

Achieving optimal treatment will require a true collaboration between general practitioners and specialist nephrologists.

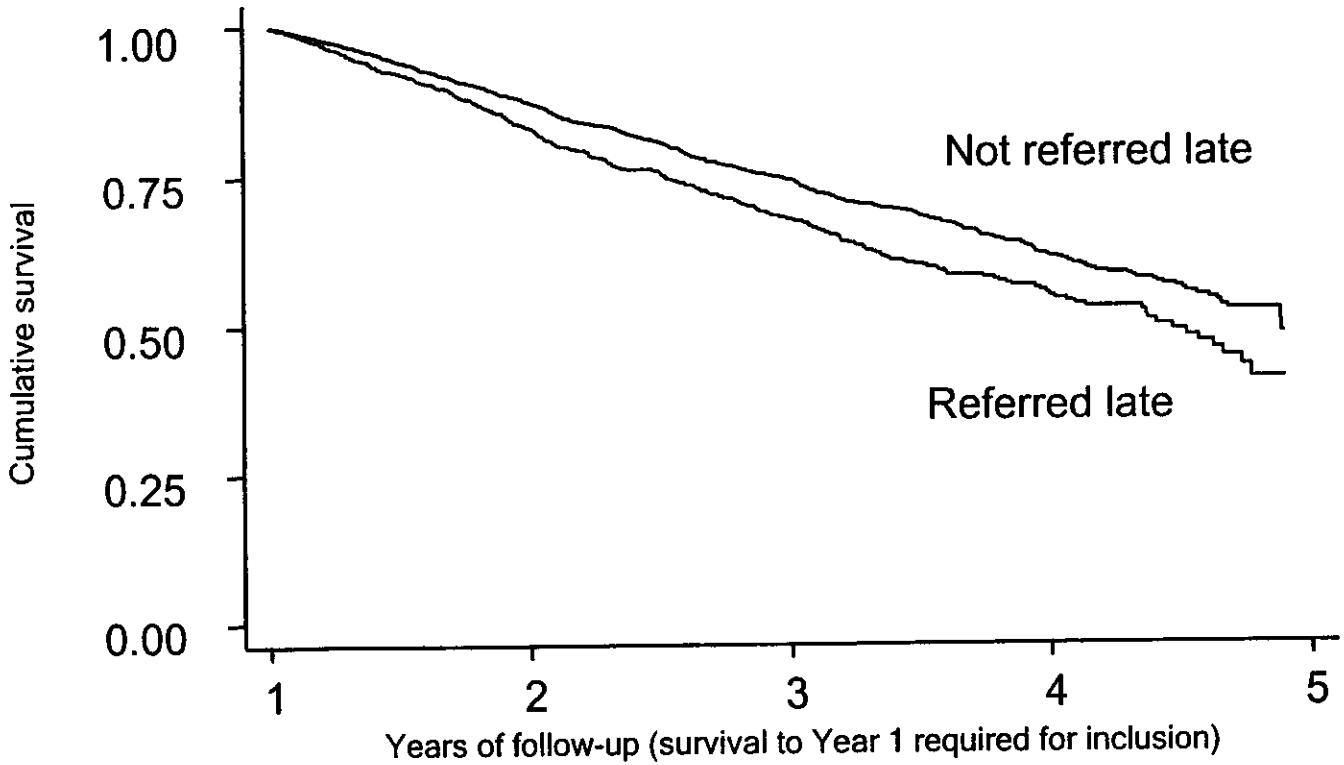
Table 5.1: Patient characteristics at the start of renal replacement therapy*

	Not Referred Late (n = 3102)	Referred Late (n = 1141)
Age (y)		
Mean ± SD	56.8 ± 15.6	56.1 ± 16.1
Range	0.6 - 86.1	0.6 - 88.7
Sex, female	1362 (43.9)	478 (41.9)
Co-morbidities†		
Ischaemic heart disease	1183 (38.1)	454 (39.8)
Cerebrovascular disease	448 (14.4)	194 (17.0)
Peripheral vascular disease	765 (24.7)	337 (29.5)
Chronic airways disease	445 (14.4)	217 (19.0)
Diabetes mellitus	893 (28.8)	408 (35.8)
Number of co-morbidities		
0	1258 (40.6)	408 (35.8)
1	787 (25.4)	265 (23.2)
2	487 (15.7)	201 (17.6)
3	339 (10.9)	146 (12.8)
4	195 (6.3)	100 (8.8)
5	35 (1.1)	21 (1.8)
Primary renal disease		
Primary glomerulonephritis	1065 (34.3)	348 (30.5)
Diabetes mellitus	640 (20.6)	290 (25.4)
Hypertension	311 (10.0)	151 (13.2)
Polycystic disease	282 (9.1)	38 (3.3)
Analgesic nephropathy	222 (7.2)	53 (4.7)
Reflux nephropathy	163 (5.3)	25 (2.2)
Other diagnoses	264 (8.5)	121 (10.6)
Uncertain	155 (5.0)	115 (10.1)
Indigenous status		
Aboriginal	239 (7.7)	153 (13.4)

*Values listed as number (%) unless otherwise specified.

†Co-morbid illness categories are not mutually exclusive.

Figure 5.1: Kaplan-Meier Curves of Cumulative Survival by Timing of Referral



Number of patients at risk at beginning of each year of study

	Year 1	Year 2	Year 3	Year 4
LR patients	1141	704	384	132
Non-LR patients	3102	1869	909	318

CHAPTER 6: URBAN DISADVANTAGE AND DELAYED NEPHROLOGY REFERRAL IN AUSTRALIA

Publication details:

Cass A, Cunningham J, Snelling P, Wang Z, Hoy W. Urban disadvantage and delayed nephrology referral in Australia. *Health and Place*. In press.

6.1: Abstract

This paper explores the relationship between area-level measures of social disadvantage and the late referral of patients with end-stage renal disease (ESRD) to a nephrologist. Patients who were referred late were those who needed to commence dialysis within three months of referral to a nephrologist. Late referral has been associated with increased morbidity and mortality. We studied 3,334 patients who started ESRD treatment in Australian capital cities between 1 April 1995 and 31 December 1998. The proportion referred late varied between areas, was higher in areas of greater disadvantage and was significantly related to the age and sex standardised incidence of ESRD. This may indicate inequitable access to optimal pre-ESRD care.

6.2: Introduction

Dialysis or transplantation is needed to keep patients with end-stage renal disease (ESRD) alive. The national renal registries of the USA, Canada, Japan and Australia/New Zealand have reported an increasing incidence of ESRD of between 3-8% per annum and increasing prevalence of between 5-7% per annum between 1993 and 1997.[52] As many as 20% of people receiving dialysis die each year.[54] Late referral to a nephrologist, a potentially avoidable factor, is associated with worse long-term survival on dialysis.[62] The association persists even after adjusting for age, severity of coexisting illnesses and functional capacity.[62] Previous reports have shown that late referral is associated with increasing age and co-existing illnesses[60,76] and ethnicity.[61] There have been no studies of the relationship between socioeconomic disadvantage and late referral for nephrology care, but an association between socioeconomic disadvantage and late presentation of glaucoma has recently been demonstrated.[77]

In this study in Australian capital cities, we investigated the association between area level measures of socioeconomic disadvantage and the proportion of ESRD patients who were referred late (LR %). We also investigated the association between the age- and sex-standardised incidence of ESRD and LR%. A positive relationship between disadvantage and late referral may indicate unequal access to optimal pre-ESRD care.

6.3: Methods

ESRD database

The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) maintains a database of ESRD patients treated in Australia. Australian federal and state governments and the Australian Kidney Foundation provide funding to the registry. All Australian renal units participate in the registry. The only patients not registered are the few who die before being established on a maintenance dialysis or transplant program.[26] Thus, it appears that the registry provides as complete a record as possible of treated ESRD patients in Australia.

Data

We analysed registry data concerning timing of nephrology referral and postcode of residence at the start of treatment. Patients who were referred late were those who needed to commence dialysis within three months of referral to a nephrologist. The approach used in this study is consistent with international nephrology research,[58,59,63,78,79] and reflects the minimum time required to provide education regarding treatment options and to establish permanent vascular access for haemodialysis. We used postcode of residence at the start of treatment as an indicator of the patient's usual place of residence before starting treatment. We restricted the analysis to Australian capital cities, as renal units are concentrated in capital cities and patients who live in capital cities should not need to move home to receive treatment. The postcode of residence at the start of treatment of each patient in this study should therefore reflect his or her usual place of residence.

Patients

Between 1 April 1995 and 31 December 1998, 3,492 patients started treatment in capital cities. We excluded 36 patients (1.0%) who had previously started treatment outside Australia or who were overseas visitors. For the

calculation of the LR%, we excluded a further 122 patients (3.5%) with ESRD caused by diseases that typically have a very short course from inception to ESRD (e.g. rapidly progressive glomerulonephritis). For such patients, referral to renal services more than 3 months before commencing treatment would not usually be possible, and late referral would thus be unavoidable.

Geography

We used Statistical Sub-Divisions (SSDs), as defined in the Australian Standard Geographical Classification,[50] as our geographical units for analysis. SSDs aggregate to form Statistical Divisions, which aggregate to form the six states and two territories. We assigned patients to areas using postcode-to-SSD concordances provided by the Australian Bureau of Statistics (ABS). We aggregated SSDs within Darwin, Canberra, and parts of Brisbane, due to the small population size of SSDs within these capital cities.

Renal units providing dialysis services were located in 23 (50%) of the 46 geographical areas we studied. Late referral was not related to geographical access to dialysis services. 26.0% of patients in areas lacking dialysis services were referred late, compared with 27.1% of patients in areas with dialysis services ($p = 0.49$).

Measurement of socio-economic status

Individual-level socio-economic data are not collected by ANZDATA. We therefore used SSD-level socio-economic data from the 1996 Census. The ABS has developed an Index of Relative Socio-economic Disadvantage (IRSD) to describe the socio-economic characteristics of an area. The IRSD is derived from attributes such as income, educational attainment, unemployment and occupations.[51] Index scores are standardised to a national mean score of 1,000; greater disadvantage is indicated by lower index values.

Statistical analysis

We calculated Pearson correlation coefficients to determine the association between LR% and IRSD values, and between LR% and the age- and sex-standardised incidence ratio (SIR) for ESRD, for all 46 capital city regions included in the study. These analyses were weighted according to the number of ESRD cases per region. We used indirect standardisation to calculate the SIR with 95% confidence intervals for ESRD for each region. Rates for the total Australian resident population were used as the reference. We used counts from the 1996 Census based on place of usual residence (ABS special tabulation request) as population denominators. Statistical analysis was performed using Stata (Release 7.0, College Station, Texas, 2000).

Ethical approval

We obtained ethical approval for the study from the ANZDATA Registry and the joint institutional ethics committee of the Royal Darwin Hospital and the Menzies School of Health Research.

6.4: Results

Of the 3,334 patients included in the study, 889 (26.7%) were referred late. The LR% varied markedly between geographical areas, with a range from 13.6 to 43.7% (Table 6.1). The average number of ESRD cases per region was 72 (range 18 to 221).

Mapping reveals areas of the capital cities with relatively high LR%. These areas were generally areas of relative disadvantage. In Sydney, areas with relatively high LR% were clustered in the south-west (Figure 6.1). In Melbourne, higher LR% areas were not contiguous, with Inner Melbourne, Northern Outer Melbourne and two southern SSDs having higher LR% (Figure 6.2). Distribution of LR% in Brisbane, Adelaide and Perth is shown in Figures 6.3–6.5, respectively.

Darwin had the highest LR% of any capital city area (43.7%). The Darwin region is different from the other capital city regions. It is small, relatively isolated, and has a higher proportion of Indigenous people in the urban population (9.5% compared with 1.0% in all major urban areas), [31] as well as a much higher proportion of Indigenous people among ESRD patients (69.0% compared with 3.5% of the total 3,334 ESRD cases).

There was a significant correlation ($r = -0.36$, $p = 0.01$) between the LR% and the IRSD (Figure 6). This indicates that a higher proportion of patients in areas of greater disadvantage were referred late. There was also a significant correlation ($r = 0.56$, $p = 0.0001$) between the LR% and the SIR for ESRD. Areas with a higher incidence of ESRD in population terms were also areas with a higher proportion of patients who were referred late.

6.5: Discussion

This study found marked variation in the proportion of ESRD patients in Australian capital cities who were referred late to nephrologists. This variation was evident in each capital city of sufficient population size to allow analysis at a SSD level. Due to the small numbers of ESRD cases occurring in the four-year study period (cases per region ranged from 18 to 221), we were unable to examine variation at a geographical level below SSD. The study also found an association between an area level measure of disadvantage and delayed referral of ESRD cases. The analysis included the capital cities of all Australian states and territories, in which approximately 63% of the total Australian population live.

Without individual-level measures of disadvantage, such as education level, income and non-English-speaking background, it is not possible to draw definite conclusions about the reasons for the greater risk of late referral in disadvantaged areas, or the relative importance of individual compared to area-level factors. Area-level measures are often perceived as imperfect proxies for individual-level measures of disadvantage, which are believed to directly affect health-seeking behaviours and health outcomes. However, community level exposures, in their own right, may directly influence access to health services. There may be poorer availability and accessibility of health services in disadvantaged areas. Patients may fail to present to primary care during the course of progressive renal insufficiency or fail to be referred promptly to a nephrologist. Issues of access, availability and quality of care are all potentially relevant.

We did not have data allowing us to determine the particular barriers to accessing nephrology services for individual patients. Timing of referral is generally determined by general practitioners or consultant physicians.[70] Avoidable late referral may be a result of those doctors' lack of awareness of the severity of a particular patient's renal insufficiency.[70,80] Late referral may stem from uncertainty regarding the appropriateness of dialysis for a given

patient[70] or perceived difficulties in the provision of ESRD treatment relating to the accessibility of services. Key factors identified as delaying referral have included lack of knowledge of guidelines regarding timing and indications for referral of ESRD patients and inadequate communication between nephrologists and primary care physicians.[71]

There are potential sources of bias in this analysis. The addresses recorded for a few patients commencing dialysis may not have indicated their place of usual residence. Patients living in capital cities were close to renal units, and were unlikely to have moved to live closer to one in order to start ESRD treatment. By contrast, patients in non-capital city areas, especially away from regional centres, may have been obliged to move in order to attend a renal unit. For these reasons, we confined our study to patients recorded as living in capital cities.

However, a potential for error remains. It is possible that a capital city address might have been recorded for some patients from non-capital city areas if they commenced dialysis at a capital city renal unit. Many of these patients would have been housed in hospital-arranged accommodation near the renal unit. We believe that the number of misclassified patients is likely to be small, because the proportion of ESRD patients with non-capital city area postcodes accorded with the proportion of all Australians who were living in non-capital city areas at the time of our study. Furthermore, the majority of renal units in capital cities, 23 of a total of 33 (70%), were located in areas of relative advantage (with an IRSD score greater than 1000). Therefore, coding errors related to temporary relocation to capital cities would be likely to understate, rather than exaggerate the incidence of ESRD observed in disadvantaged areas. We have no evidence that patients who did move to start treatment differed in relation to their likelihood of being referred late. There is no significant difference in the proportion referred late between those who have capital city postcodes and those who have non-capital city postcodes (26.7% v. 28.4%, $p = 0.16$). For these reasons, we believe that any residential

classification errors should not have significantly affected the relationship between late referral and disadvantage.

This study included 118 Indigenous ESRD cases (3.5%). We have previously presented analysis showing that postcode of residence at the start of treatment may be less valid as an indicator of place of usual residence for Indigenous patients,[24] but appears to be adequate for non-Indigenous patients.[36] In the current study there were only seven SSDs in which Indigenous cases constituted more than 5% of total cases. We repeated the analysis using data regarding the previous place of usual residence rather than postcode at the start of treatment, for Indigenous patients in the seven SSDs. The associations between disadvantage and delayed referral, and between delayed referral and the standardised incidence of ESRD remained strong and statistically significant.

Differential quality of reporting regarding late referral could potentially bias the results. However, all renal units that provide ESRD treatment in Australian participate fully in the registry.[26] Considerable debate in the Australian and international nephrology communities about late referral[63] is evidence of heightened awareness of this issue. In this study, late referral was defined as needing to commence dialysis within three months of referral to a nephrologist. The data were collected as a categorical variable (yes/no) by ANZDATA. We could not analyse the actual time between referral and commencement of treatment as a continuous variable. Such a categorical definition is, however, fairly standard in the international literature,[58,59,63,78,79] and reflects clinical considerations regarding preparation for ESRD treatment.

This study found a strong association between the proportion of ESRD patients referred late to a nephrologist and the age- and sex-standardised incidence of ESRD. We have previously demonstrated that disadvantaged areas have a higher standardised incidence of ESRD.[36] Thus, disadvantaged areas have both an increased population burden of ESRD and also a greater risk of delayed access to specialist renal services among those with disease,

this delay being associated with a poorer outcome. It is important to explore the extent to which unequal access to primary health care and inadequate communication between nephrologists and primary care doctors regarding appropriate timing and indications for referral influence the higher proportion of patients referred late in disadvantaged areas.

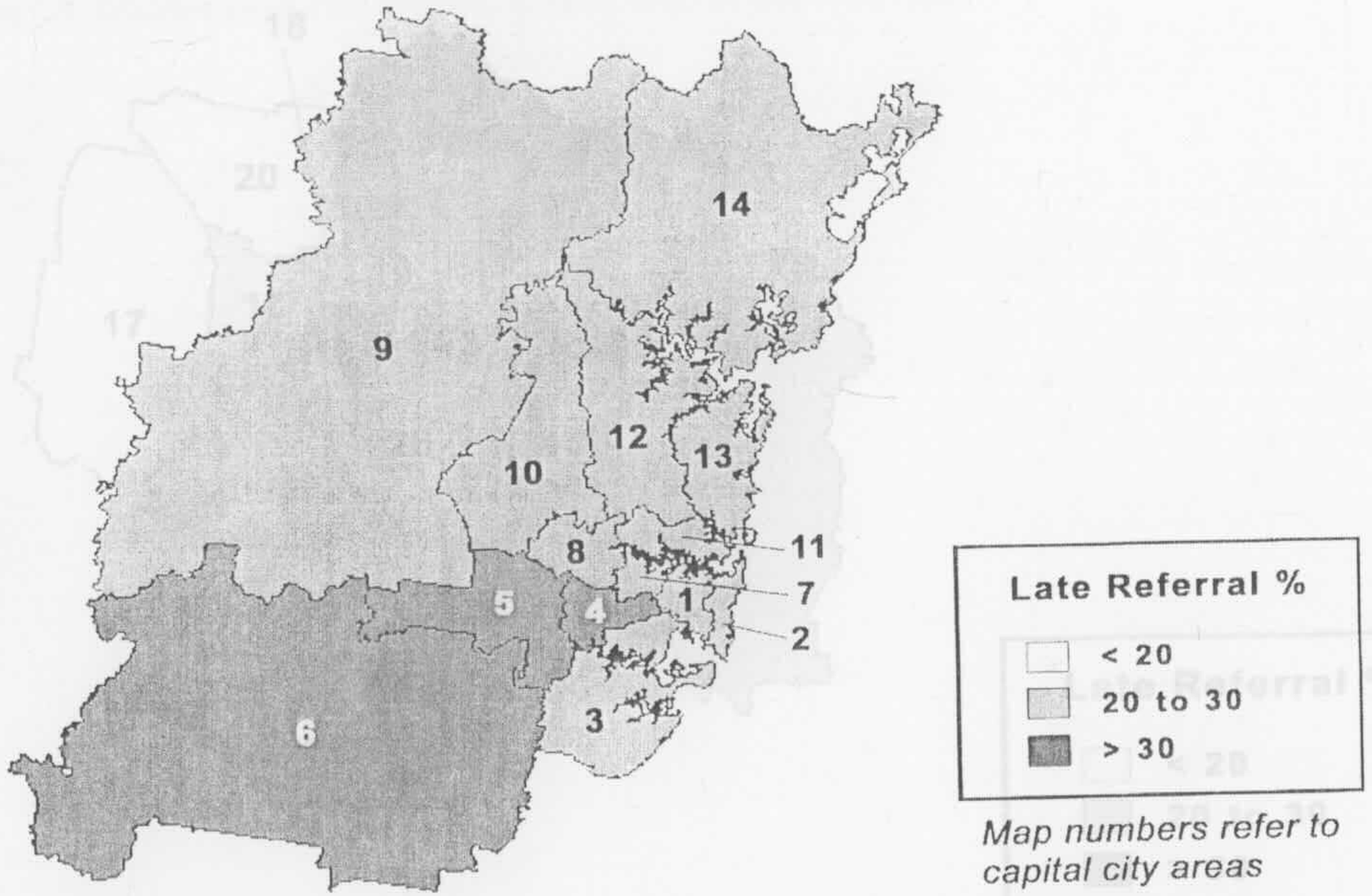
The incidence and prevalence of ESRD is increasing throughout the developed world. It is a condition with a significant impact on quality of life, on life expectancy, and on health expenditures. Higher rates of ESRD have been documented in minority ethnic groups throughout the developed world.[11,81-83] The risk of end-stage renal disease is elevated among people with a number of increasingly common chronic conditions, such as diabetes and hypertension. Nevertheless, a list of guidelines for prevention activities in general practice recently circulated to all Australian general practitioners,[84] did not include a section on kidney disease; nor did it suggest anywhere the need for urine screening for signs of early renal disease. Despite growing emphasis on reducing health inequalities[5,18] and overall improvement in the prevention and care of chronic diseases, we are currently failing, with regard to chronic renal failure, to address the needs of general practitioners and the public, especially in disadvantaged areas.

Table 6.1: Late referral proportion of ESRD cases in Australian Capital Cities 1995–1998

City	Area (map references)	Population	Cases	LR% (95% CI)
Sydney	Inner Sydney (1)	255,499	115	25.2 (16.9–36.2)
	Eastern Suburbs (2)	227,080	66	22.7 (12.7–37.5)
	St George-Sutherland (3)	393,497	94	22.3 (13.8–34.1)
	Canterbury-Bankstown (4)	290,138	122	33.6 (24.1–45.6)
	Fairfield-Liverpool (5)	302,046	154	40.3 (30.9–51.6)
	Outer South Western Sydney (6)	209,973	55	38.2 (23.6–58.4)
	Inner Western Sydney (7)	147,774	57	26.3 (14.7–43.4)
	Central Western Sydney (8)	268,683	75	29.3 (18.4–44.4)
	Outer Western Sydney (9)	293,242	60	25.0 (14.0–41.2)
	Blacktown-Baulkham Hills (10)	352,697	95	22.1 (13.7–33.8)
	Lower Northern Sydney (11)	264,779	79	22.8 (13.5–36.0)
	Hornsby-Ku-ring-gai (12)	236,562	69	29.0 (17.7–44.8)
	Northern Beaches (13)	212,387	46	23.9 (11.9–42.8)
	Gosford-Wyong (14)	263,055	102	20.6 (12.7–31.5)
Melbourne	Inner Melbourne (15)	215,427	75	40.0 (27.0–57.1)
	Western Melbourne (16)	389,408	134	26.1 (18.2–36.3)
	Melton-Wyndham (17)	113,637	19	15.8 (3.3–46.1)
	Moreland City (18)	131,082	56	25.0 (13.7–41.9)
	Northern Middle Melbourne (19)	235,942	99	23.2 (14.7–34.9)
	Hume City (20)	116,441	44	18.2 (7.9–35.8)
	Northern Outer Melbourne (21)	157,779	46	37.0 (21.5–59.2)
	Boroondara City (22)	146,657	27	22.2 (8.2–48.4)
	Eastern Middle Melbourne (23)	396,342	116	25.9 (17.5–36.9)
	Eastern Outer Melbourne (24)	225,159	44	27.3 (14.1–47.6)
	Yarra Ranges Shire Part A (25)	132,303	32	21.9 (8.8–45.1)
	Southern Melbourne (26)	364,925	110	19.1 (11.8–29.2)
	Greater Dandenong City (27)	126,887	51	29.4 (16.5–48.5)
	South Eastern Outer Melbourne (28)	186,260	42	21.4 (9.8–40.7)

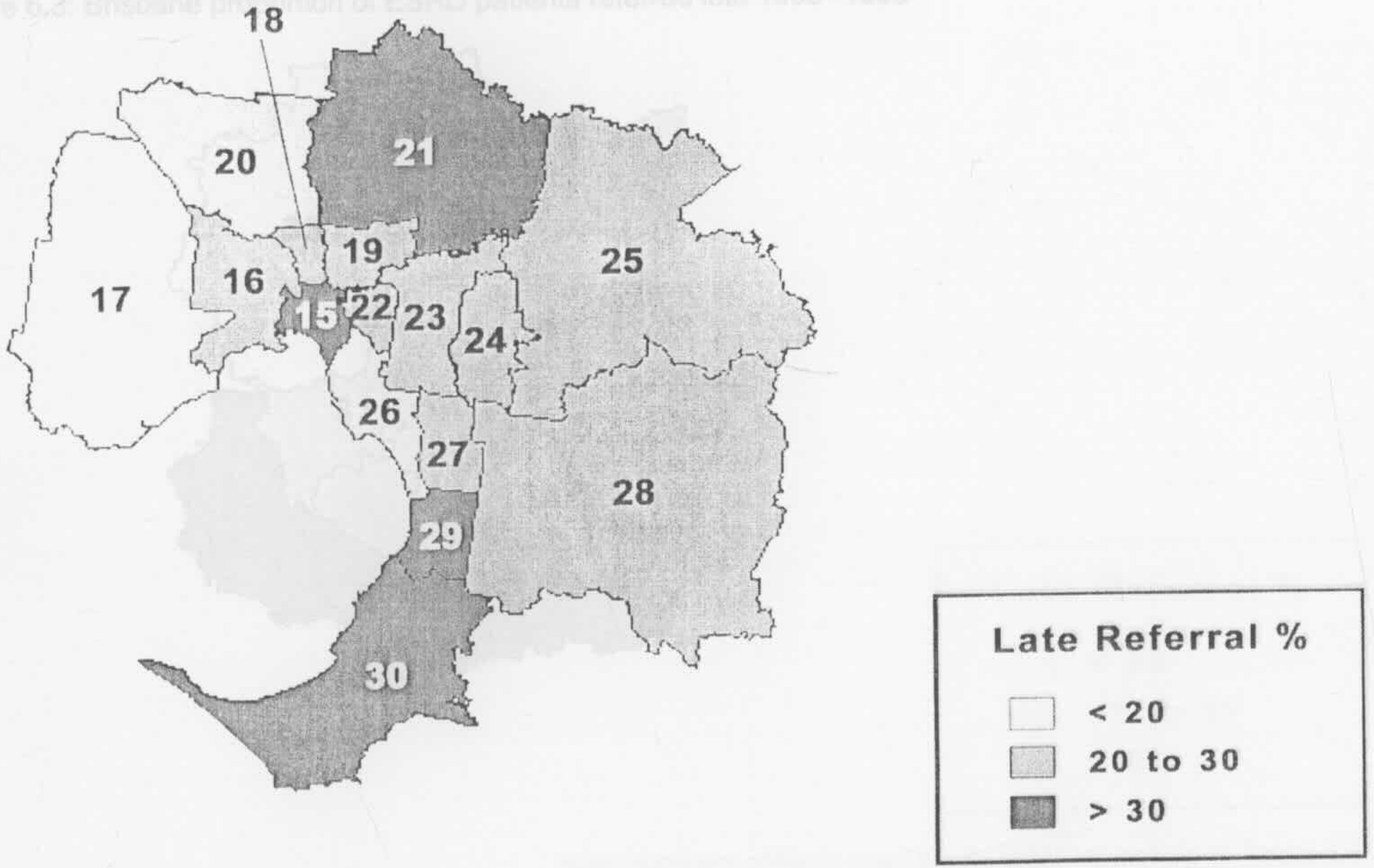
	Frankston City (29)	105,728	18	33.3 (12.2–72.5)
	Mornington Peninsula Shire (30)	114,183	38	31.6 (16.3–55.2)
Brisbane	Brisbane City (31)	791,840	221	21.7 (16.0–28.8)
	South West Brisbane (32)	336,574	72	33.3 (21.4–49.6)
	North Brisbane (33)	245,978	48	16.7 (7.2–32.8)
	Redland Shire (34)	100,135	22	13.6 (2.8–39.8)
Adelaide	Northern (35)	327,224	89	24.7 (15.5–37.4)
	Western (36)	202,917	88	25.0 (15.7–37.8)
	Eastern (37)	211,655	40	30.0 (15.5–52.4)
	Southern (38)	308,391	75	25.3 (15.3–39.6)
Perth	Central Metropolitan (39)	111,680	33	18.2 (6.7–39.6)
	East Metropolitan (40)	205,454	50	28.0 (15.3–47.0)
	North Metropolitan (41)	379,721	106	26.4 (17.6–38.2)
	South West Metropolitan (42)	255,278	56	25.0 (13.7–41.9)
	South East Metropolitan (43)	289,519	92	33.7 (22.9–47.8)
Hobart	Hobart (44)	191,136	54	27.8 (15.5–45.8)
Darwin	Darwin (45)	78,397	71	43.7 (29.7–62.0)
Canberra	Canberra (46)	297,943	77	15.6 (8.1–27.2)

Figure 6.1: Sydney proportion of ESRD patients referred late 1995–1998



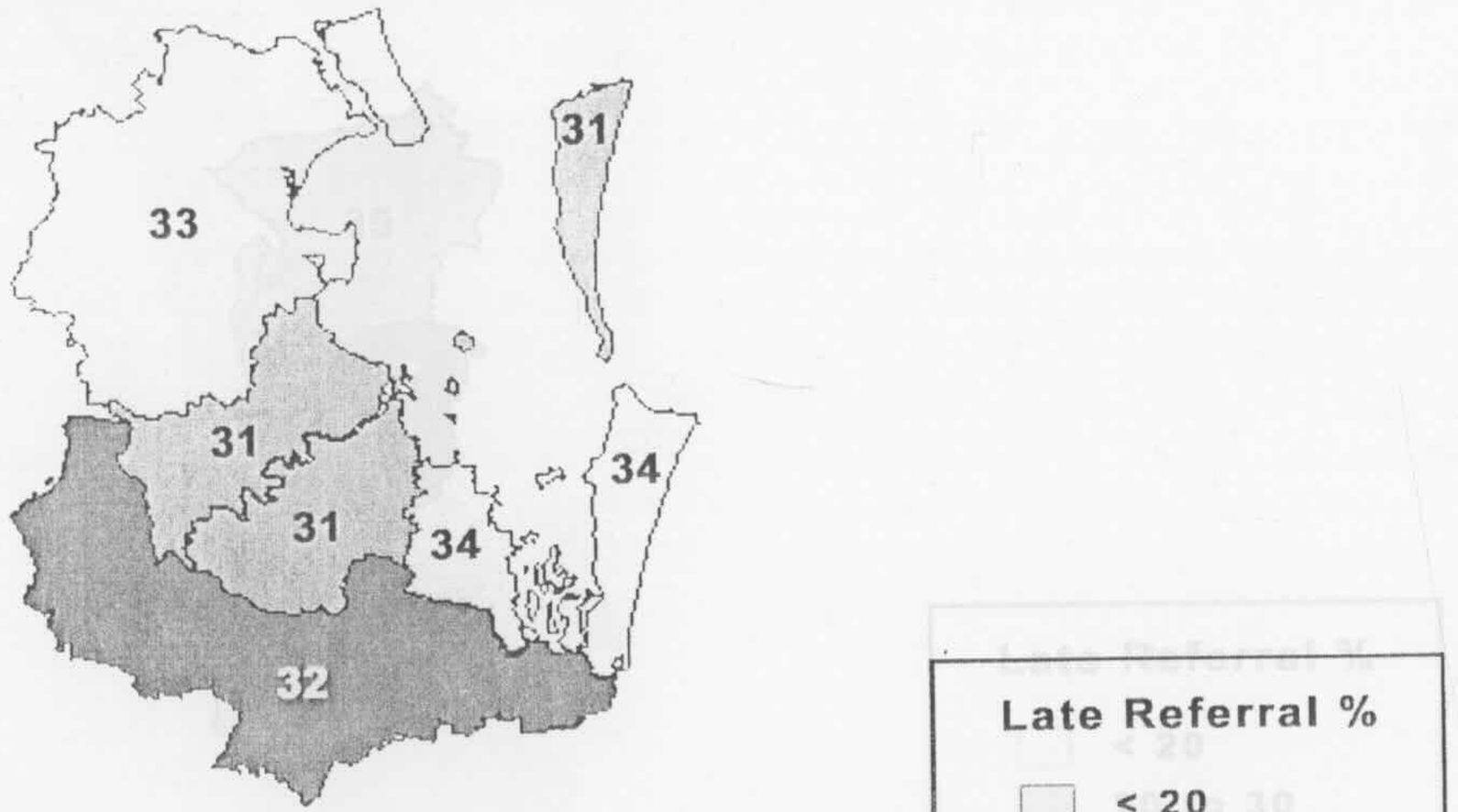
Map numbers refer to capital city areas specified in Table 6.1

Figure 6.2: Melbourne proportion of ESRD patients referred late 1995--1998



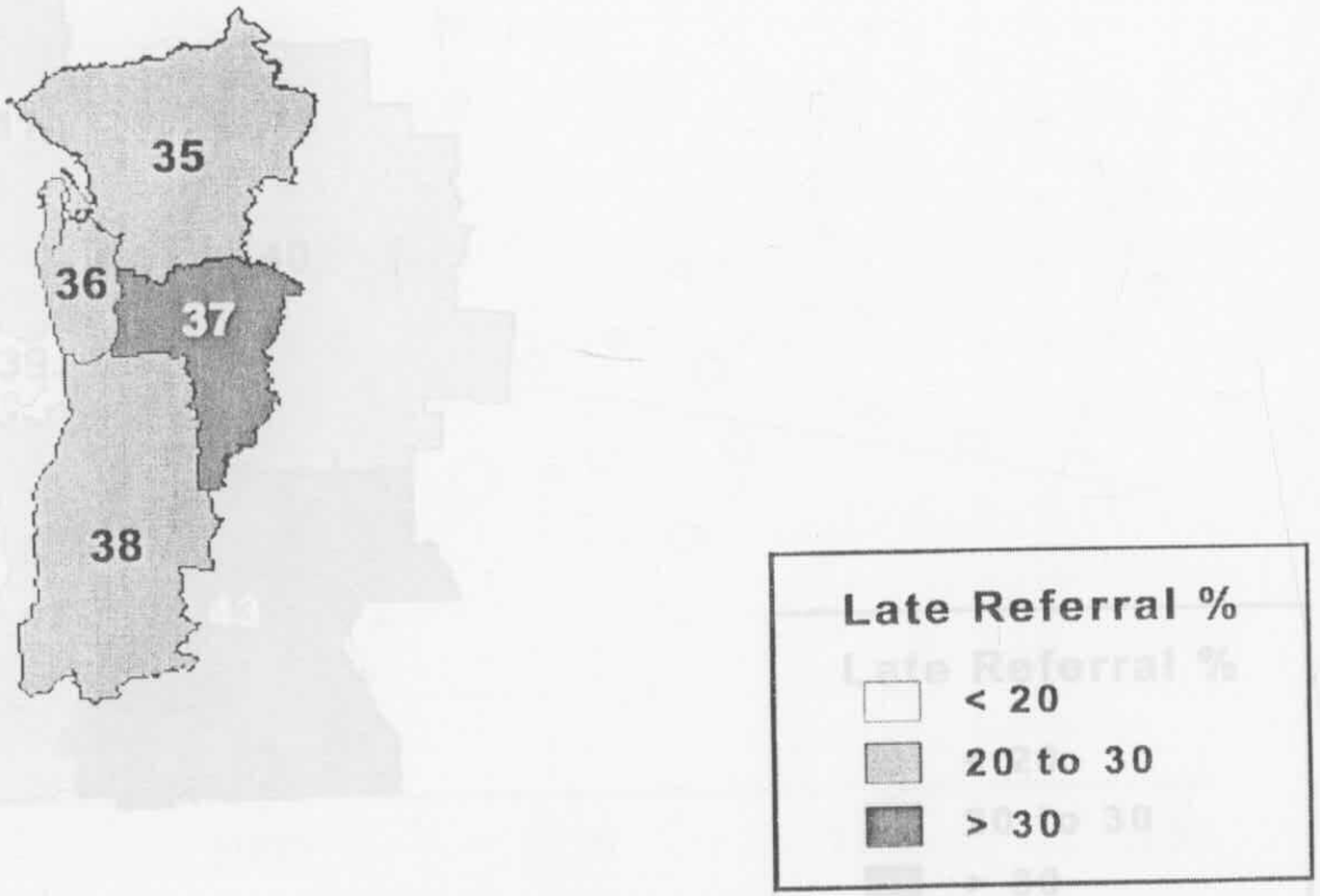
Map numbers refer to capital city areas specified in Table 6.1

Figure 6.3: Brisbane proportion of ESRD patients referred late 1995--1998



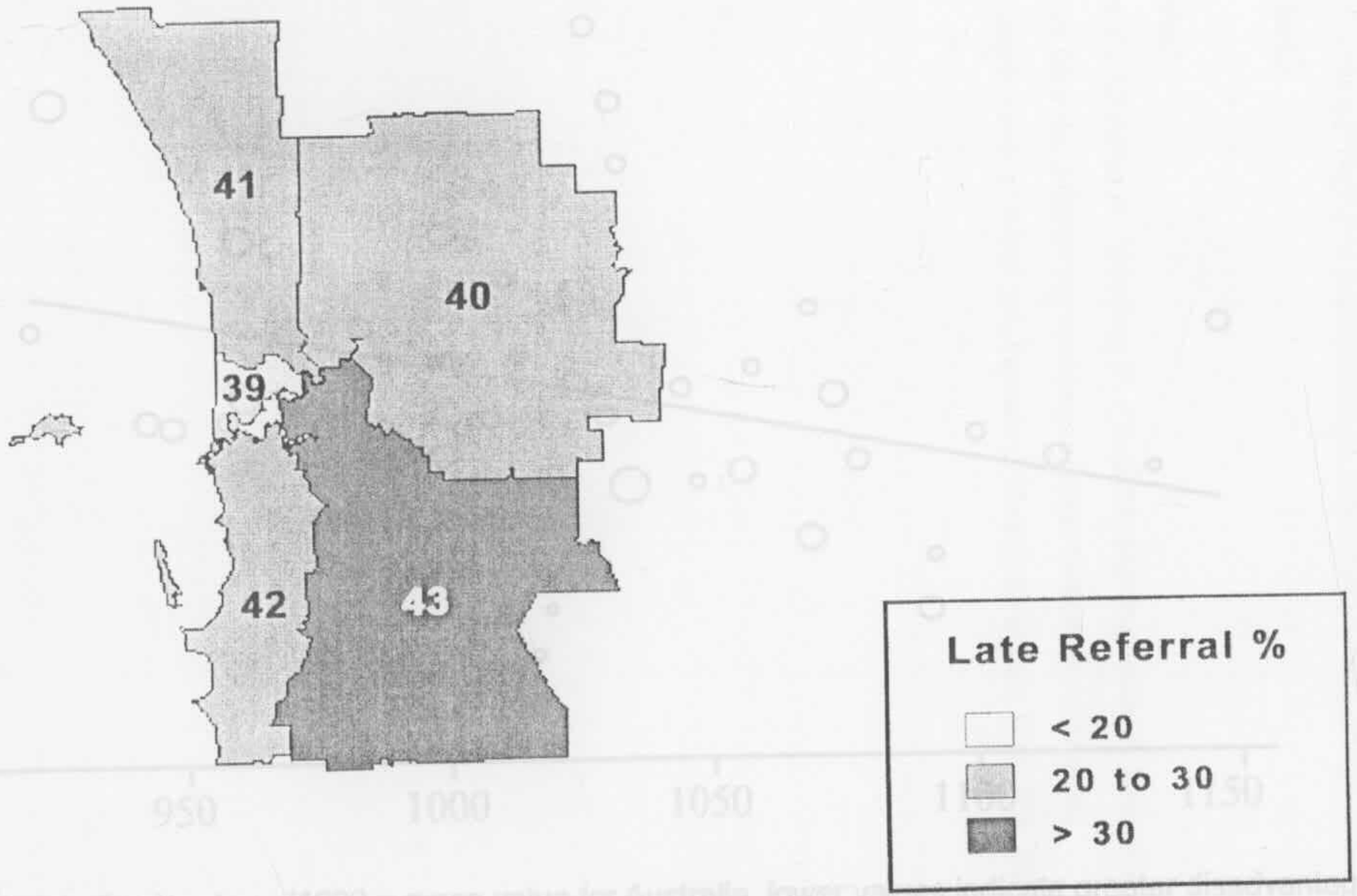
Map numbers refer to capital city areas specified in Table 6.1

Figure 6.4: Adelaide proportion of ESRD patients referred late 1995--1998



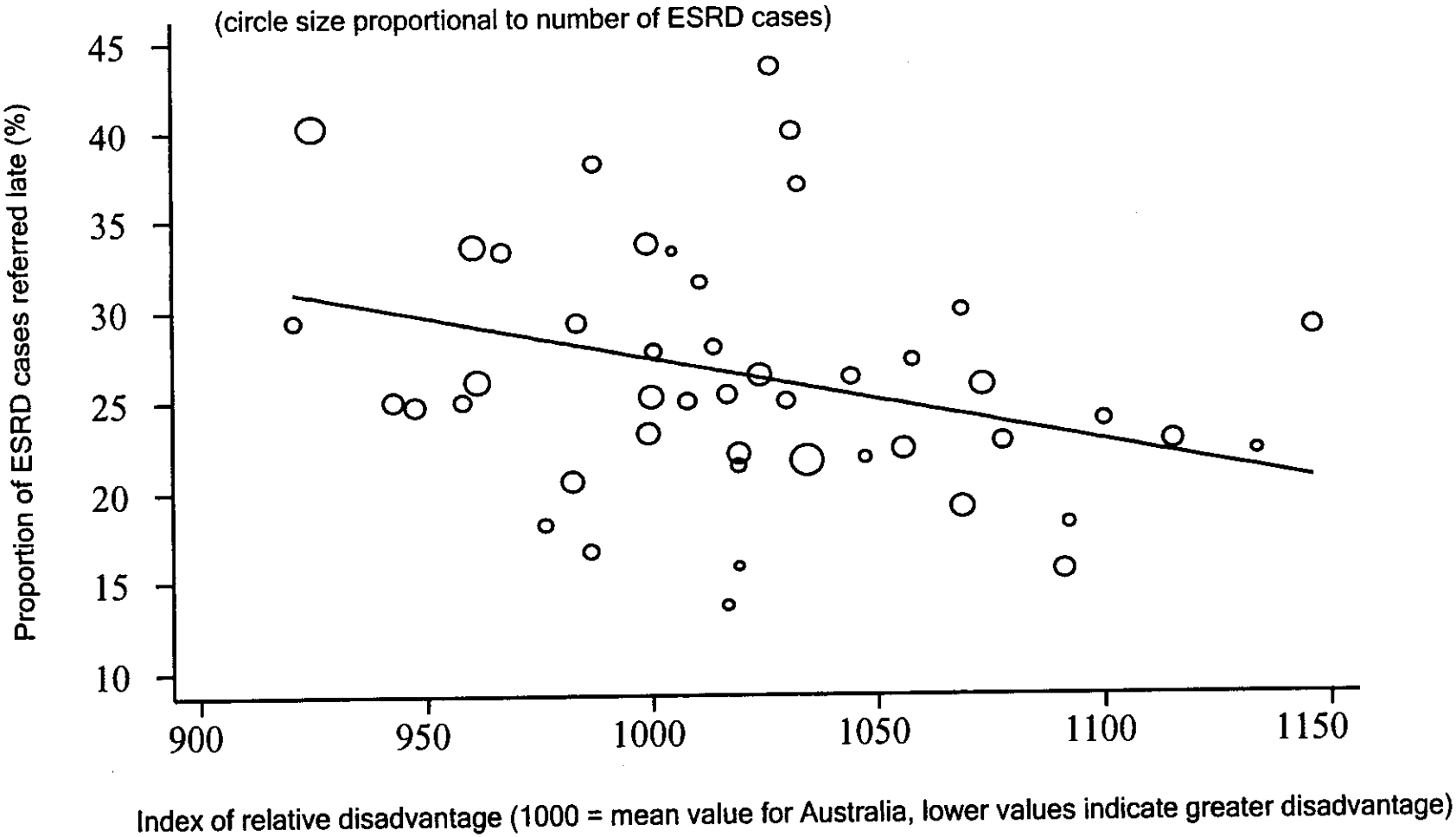
Map numbers refer to capital city areas specified in Table 6.1

Figure 6.5: Perth proportion of ESRD patients referred late 1995--1998



Map numbers refer to capital city areas specified in Table 6.1

Figure 6.6: Socioeconomic Disadvantage and Late referral of ESRD cases by SSD



CHAPTER 7: SHARING THE TRUE STORIES: IMPROVING COMMUNICATION BETWEEN ABORIGINAL PATIENTS AND HEALTH CARE WORKERS

Publication details:
Cass A, Lowell A, Christie M, Snelling P, Flack M, Marrnganyin B, Brown I. Sharing the true stories: improving communication between Aboriginal patients and health carers. *Medical Journal of Australia* 2002; 176 (10): 466-470.

7.1: Abstract

Objectives: To identify factors limiting the effectiveness of communication between Aboriginal patients with end-stage renal disease (ESRD) and health care workers, and to identify strategies for improving communication.

Design: Qualitative study, gathering data through (a) videotaped interactions between patients and staff and (b) in-depth interviews with all participants, in their first language, about their perceptions of the interaction, their interpretation of the video record and their broader experience with intercultural communication.

Setting: A satellite dialysis unit in suburban Darwin, Northern Territory. The interactions occurred between March and July 2001.

Participants: Aboriginal patients from the Yolngu language group of North East Arnhem Land and their medical, nursing and allied professional carers.

Main outcome measures: Factors influencing the quality of communication.

Results: A shared understanding of key concepts was rarely achieved. Miscommunication often went unrecognised. Sources of miscommunication included: lack of patient control over the language, timing, content and circumstances of interactions; differing modes of discourse; dominance of biomedical knowledge and marginalisation of Yolngu knowledge; absence of opportunities and resources to construct shared understanding; cultural and linguistic distance; lack of staff training in intercultural communication; and lack of involvement of trained interpreters.

Conclusions: Miscommunication is pervasive. Trained interpreters provide only a partial solution. Fundamental change is required for Aboriginal patients to have significant input into the management of their illness. Educational resources are needed to facilitate a shared understanding, not only of renal physiology, disease and treatment, but also of the cultural, social and economic dimensions of the illness experience of Aboriginal people.

7.2: Introduction

Doctor-patient communication, by creating good interpersonal relationships, allowing the exchange of information and facilitating treatment-related decisions, is fundamental to optimal medical care.[85] Effective communication correlates with improved outcomes, including physiological criteria such as levels of blood pressure and blood sugar.[86] Conversely, professional, language and cultural barriers can impede communication.[87,88]

Few investigators have studied the extent and consequences of miscommunication in Australian Aboriginal health care,[89] an area in which effective communication is extremely important.[90] Previous studies involving interviews with service providers and Aboriginal patients have identified significant concerns about communication.[16,91,92] Some researchers have identified an acceptance, as the *norm*, of a grossly deficient standard of cross-cultural communication.[16] We believe that previous studies, based as they have been on indirect reporting or simulated interactions[93] (rather than direct observation and analysis of the interaction itself), probably understate the degree of miscommunication. The communication gap may be so wide, and so ingrained in health care, that it is not even perceived by staff.[94] Similar misunderstandings in Australian court cases often go unrecognised by the participants.[95]

In our study of staff-patient interactions in a dialysis unit in Darwin, NT, we attempted to develop a more informed understanding of intercultural communication between Aboriginal patients and non-Aboriginal staff and to devise strategies for improvement.

7.3: Methods

Participants and setting

The participants were patients and staff of a satellite dialysis unit in suburban Darwin. The interactions on which our study is based occurred between March and July 2001. The patients came from the Yolngu language group in north-east Arnhem Land. Five interactions were videotaped, each involving a single patient (although family members were present on two of these occasions). Four interactions involved a single staff member and one involved a doctor and a nurse. The interviews occurred at the dialysis unit and at a remote Aboriginal community several hundred kilometres from Darwin.

Design

We used qualitative research methods to reflect the perspectives of all participants. The research design drew on 'grounded theory', which describes the inductive process of identifying analytic categories to describe and explain key issues as they emerge from data.[96] Hypotheses were developed from the ground up, rather than being defined *a priori*, as is usually done in quantitative research.

Recognising that the effectiveness of communication is inextricably connected with structural issues of poverty, dispossession, marginalisation, low educational achievement and racial discrimination,[91] we chose a 'participatory action' approach. This is a style of research in which the demarcation between 'researcher' and 'subject' is blurred, research design is negotiated, and the participants perceive the need to change and are willing to participate actively in the change process.[97] The research process is illustrated in Figure 7.1.

Sampling

Five clinical interactions, identified beforehand in consultation with both patients and staff, were selected. They concerned diagnosis, treatment and chronic disease management. Staff were asked to follow their usual practice

regarding the use of interpreters. The interactions included two medical reviews (one with a patient on regular haemodialysis and one with a patient with chronic renal disease close to needing maintenance dialysis), two education sessions (a nurse providing feedback on blood-test results and a consultation between an allied health professional and a new patient), and an interaction between a nurse and a patient during dialysis.

We selected participants using a 'maximum variation sampling approach', wherein a small sample is selected to reflect maximum diversity across specified attributes.[98] The participants covered as wide a range as possible in terms of age, sex, duration of renal experience (receiving or providing treatment), degree of familiarity with the culture and language of the other group, and experience in cross-cultural communication.

Collection of data

The five interactions were videotaped and analysed by all participants, the research team and professional interpreters. Multi-layered descriptions of the interactions were constructed from these varied perspectives.

After each interaction, the participants were interviewed separately, in their first language, to explore their perceptions of the effectiveness of the communication. The post-interaction ("exit") interviews were conducted by AL (for English speakers) and BM (for Yolgnu speakers). Semi-structured, in-depth interviews were also conducted with most staff and patients to develop a greater understanding of their backgrounds and wider experience.

Informed consent was obtained from all participants before videotaping. BM obtained verbal and written consent in the patients' own language.

Analysis

The data from all sources were integrated to explore the extent of miscommunication; the cultural, linguistic and systemic factors influencing

communication; the effectiveness of communication strategies being used; and possible strategies for improving communication.

The video descriptions and interview transcripts were entered into QSR NVIVO, a computer software package which assists in managing qualitative data. Categories used in analysis were derived primarily from the data and through sequential analysis. To strengthen the validity of our analysis, we used 'triangulation' (the comparison of results from two or more different methods of data collection) and 'respondent validation' (cross-checking *interim* findings with the participants).[99,100]

Ethics approval

The study was approved by the Joint Institutional Ethics Committee of the Menzies School of Health Research and Royal Darwin Hospital, and of the Northern Territory University.

7.4: Results

A picture emerged of serious miscommunication, often unrecognised by participants, regarding fundamental issues in diagnosis, treatment and prevention. Although there were many differences of goals and structure observed in the interactions, common themes relating to miscommunication emerged. Factors impeding communication included lack of control by the patient, differing modes of discourse, dominance of the biomedical model, lack of shared knowledge and understanding, cultural and linguistic distance, lack of staff training in inter-cultural communication, and failure to call on trained interpreters (see Figures 7.2 and 7.3).

Lack of control by the patient

In each interaction, it was the *staff* who controlled the time, place, participants, purpose, structure, topics and language, as well as the form and style of discourse. There were few opportunities for the patients to initiate or influence the agenda. The staff decided whether or not interpreters would be required, even when unaware of the patient's fluency in English.

Differing modes of discourse

Western modes of discourse dominated, with Yolngu modes being marginalised or excluded. Question and answer routines, central to western discourse, do not feature commonly in Yolngu discourse, particularly in relation to personal topics. In Yolngu discourse, the question and answer approach is complicated by factors such as cultural restrictions on who may ask for, or give, specific information. It is generally considered impolite to directly contradict or to respond negatively, particularly in encounters of unequal power or when the participants lack a close relationship. The patients in our study repeatedly gave responses that they believed the staff wanted to hear, a practice known in linguistics as "gratuitous concurrence".[101] Triangulation showed that these responses did not represent the patient's true

feelings or experience, but were attempts to give 'required' or 'correct' responses, as in the following example:

Physician: How much are you drinking? How much water?

Patient: Little bit water tea, little bit ga bilin ("that's it").

Physician: How much each day? Water, tea?

Patient: Three cup, two cup, little bit (said very confidently).

The physician believed that the patient had a clear understanding of the question and was describing the amount of fluid drunk daily. However, it later became clear that the patient responded this way because she knew what was expected. Her understanding of fluid restriction was that she should drink only two cups of "fizzy drink" per day, but that drinking tea or water whenever she felt like it was acceptable. Questions requiring a "yes"/"no" response were particularly susceptible to gratuitous concurrence. A nurse made the following comment:

I never even considered that they might be saying "yo" (yes) when they are really saying "no", I never even thought of it.

Dominance of the biomedical model

The discourse in the interactions focused on renal function, renal failure, monitoring of and adherence to dialysis, and dietary and medication regimens. Non-medical aspects were excluded or marginalised. Yolngu priorities, which emerged in subsequent interviews and informal discussions, were social, cultural and economic, relating primarily to (currently) unavoidable re-location to Darwin if patients wished to access necessary treatment. One patient illustrated her problems with living in Darwin:

I told her (the staff member) the truth – that I wasn't getting enough (food). When I get my allowance, they take all the money for accommodation and leave only $30 for food – that's not enough

Yolngu priorities, which directly affect clinical management, were rarely raised, and when raised, were either not pursued or were brushed aside. Patients had no explicit opportunities to discuss their own approaches to managing their health. For example, in two interactions, they attempted to talk about Yolngu

knowledge and management practices (related to traditional foods), but their contributions were either not understood or not acknowledged.

Lack of shared knowledge and understanding

Extensive prerequisite knowledge is essential for making sense of information about the management of ESRD. A shared understanding of kidney and heart function, and of the nature of the circulatory system (including, for example, the components and function of blood), is necessary for meaningful discussion about medication, fluid restriction and dialysis. As shared understanding of many of these concepts does not exist, effective communication is seldom achieved.

Cultural and linguistic distance

The vast cultural and linguistic distance between staff and patients in these interactions impeded communication. Staff use of culturally specific terminology was one difficulty. For instance, quantification was a constant problem. Key biomedical issues were expressed quantitatively, including percentage of renal function, number of drinks consumed, amount and frequency of medications, length of visits home, length of time without dialysis, high and low blood pressure, and blood test results. But litres, kilograms, hours, dates and percentages have little, if any, meaning for most Yolngu, while Yolngu ways of expressing quantity and spatial and temporal concepts were completely unknown to staff.

Lack of staff training in cross-cultural communication

None of the staff speaks an Aboriginal language and none of their Yolngu patients speaks English as a first language. Furthermore, none of the staff had received any formal training in intercultural communication. Even general cultural awareness training, which is increasingly available to staff, had been utilised to a limited extent and to minimal effect. One physician recalled his only training experience in cultural awareness:

In Alice Springs, I probably had a day's training. It would have been a standard thing, and it was brief, and I have no memory of it.

And yet he found that intercultural communication was:
an incredibly difficult aspect of working there. I knew that there was next to no communication between me and the patients, which had obvious impact on what happened.

There were organisational barriers to formal training, as a renal nurse related:
I haven't done a cross-cultural course at all. When I first came up (to Darwin,) it wasn't compulsory and I've tried to get in several times over the years and it was either booked out or Renal couldn't relieve me because they didn't have enough staff at the time.

For most of the staff, learning occurred 'on the job', but this had serious limitations, as a physician reflected:
You become aware of the issues just through doing what you're doing. This is poor. ..... you learn by obstacles and by ..... causing affront and problems.

Limited use of interpreters

Until recently, there was no alternative to attempting whatever communication was possible through the assistance of whoever was available. In the absence of professional interpreters, family members had to suffice – a seriously inadequate practice.[102] Although an Aboriginal Interpreter Service providing Yolngu language speakers now exists, changes in practice are occurring only slowly. In the interactions observed in our study, the closest any of the staff or patients came to seeking the assistance of a professional interpreter was to call on the assistance of a family member who had some informal interpreting experience.

7.5: Discussion

Our study demonstrates that renal staff and Yolngu patients rarely achieved a shared understanding of key concepts. Consequently, communication was seriously limited and quality of care compromised. There was little indication that either staff or patients had, before or during these encounters, considered the potential for miscommunication. Even if this had occurred, staff had no tools or guidelines for assessing its extent. Our findings suggest that any substantial improvement in communication, and in ensuing health outcomes, requires fundamental change in the delivery of healthcare, in particular, in the construction of a shared understanding, from the perspectives of both staff and patients, of physiological processes, renal disease and treatment options.

Previous research has been based on interviews with service providers, and sometimes with Aboriginal patients, about their perception of communication issues. Our study, by contrast, involved direct observation of interactions, and then, with the input of all participants, sequential analysis. We have shown that much miscommunication can easily go unrecognised.

While previous studies of communication breakdown have usually focussed on the clinical interaction, we looked beyond this. Our findings enabled us to understand both sides and to see the clinical interaction within the social, cultural and political context relevant to the delivery of health care to Aboriginal people.

We believe the qualitative research methods we used were appropriate. It could be argued that our findings may not be generalisable to staff-patient communication in the entire renal unit in which the research occurred, nor transferable to other patient-care settings. However, we believe that the methods of triangulation, respondent validation and maximum variation sampling techniques strengthen the validity of our findings

Videotaping the interactions did not appear to fundamentally alter the communication strategies used by staff. In any case, we would expect any bias, arising through participants' knowledge of being observed, to be towards *more* effective rather than *less* effective communication. Our results support similar findings of miscommunication in other Aboriginal health research[16,94,103] and in international cross-cultural research.[85,87] We believe that our research findings are both credible and relevant to the delivery of healthcare to Aboriginal people and that similar miscommunication problems are likely to exist in other health care settings in which there are people whose first language is not English.

Fundamental change is required to achieve effective communication with Aboriginal patients who have renal disease. We will not be able to deliver optimal care without striking a balance between the staff's medical imperatives and the patients' social needs. First, we must train staff in inter-cultural communication. It is the staff's responsibility to make this accommodation to enable Aboriginal people to make informed choices in the context of their own language and cultural environment. Second, we need to offer training to Aboriginal interpreters to prepare them for work with health care workers. Third, we should promote strategies to monitor the effectiveness of communication and to repair miscommunication. Fourth, we should develop educational resources to facilitate a shared understanding, on the one hand, of physiological processes and treatment options and, on the other, of the cultural, social and economic realities confronting Aboriginal patients and their families. Planning and implementing such strategies for the Yolngu will require collaboration between staff, patients and patients' families. We are currently developing such a project. Short of such radical change, attempts to improve communication can meet with only partial success.

Figure 7.1: The participatory action research process

Roles, methodology and research parameters negotiated by research team

↓

Research participants selected using maximum variation sampling approach

Written and verbal consent obtained*

↓

Five key interactions selected and then videotaped

↓

'Exit' interviews with participants in each interaction*

↓

Videotape analysis by research team → Feedback to participants;

and professional interpreters ← cross-checking interim findings with participants*

↓

Semi-structured, in-depth interviews with participants*

↓

Video descriptions and interview transcripts entered into software package QSR NVIVO

↓

Analytic categories and hypotheses → Feedback to participants;

derived from all data sources ← cross-checking interim findings with participants*

↓

Strategies for change developed

*Obtaining consent, exit interviews, feedback and in-depth interviews were undertaken with participants in their first language

Figure 7.2: Sample interaction (A)

Setting

The doctor's office in a remote community 500 kilometres from Darwin

Participants

Mr 'A', a 24-year-old man with chronic renal disease who recently had a prolonged admission to Royal Darwin Hospital, during which he required temporary dialysis. He lives with his mother and grandmother, and is fluent in Yolngu languages but not in English. He will need relocation to Darwin within two years for maintenance dialysis.

Dr 'B', a 38-year-old male physician with many years' experience working with multicultural and Aboriginal patients.

The interaction

The twenty-minute interaction, in English, was initiated by Dr B, who did most of the talking. The patient's mother and grandmother assisted with communication. Mr A and his family asked no questions and gave limited, non-verbal responses to B's questions.

Communication goals

Dr B had clear goals:

I wanted to reinforce that the patient was at risk of progression to ESRD and that he would benefit from treatment, of blood pressure in particular .....and treatment of other things like anaemia. .....The main thing was that he doesn't need dialysis at the moment, but that he needed to be monitored and to take his tablets.

The expectations of Mr A and his family were unclear. It later became apparent that they believed that his disease had been cured during his admission. They had no appreciation of its chronicity and of his need for regular tests and medications.

The participants' assessment

Dr B was uncertain of the outcome of the interaction:

Perhaps his mother got some idea .....I hope they at least understand he is at risk of needing more dialysis, I think they now understand he has kidneys that aren't working so well ...

After the consultation, the Yolgnu researcher discovered that the family's understanding of the doctor's advice was that Mr A should be taking medication. Despite Dr B's extended explanation of chronicity and prognosis, the interaction did not achieve a shared understanding of the state of the patient's kidneys, the significance of test results or the importance of blood pressure control. The family had understood little. This prompted the Yolgnu researcher to recall Dr B to explain further, while she provided interpreting assistance.

Consequences for clinical management

Miscommunication reduced the ability to actively engage Mr A and his family in controlling his blood pressure, in retarding progression of his renal disease and in planning for future dialysis. Lack of effective communication regarding the need to relocate to Darwin for treatment, away from family and community, could result in the patient's reluctance to accept dialysis in the future.

Figure 7.3: Sample interaction (B)

Setting

The open waiting area at the dialysis unit.

Participants

Ms 'C', a 50-year-old woman who had been on dialysis for five years. She speaks Yolgnu languages and is fluent in conversational English. She has graduate qualifications as a teacher.
Sr 'D', a 31-year-old female nurse with ten years' experience in renal services, both as nurse and patient educator, but with little formal training in cultural awareness.

The interaction

The interaction, in English, was initiated by Sr D. She determined the he timing and location to fit in with her work program and with the patient's dialysis schedule. The nurse did most of the talking and the patient asked few questions.

Communication goals

Sr D aimed to provide education through feedback and discussion of routine monthly test results. She aimed to integrate information about dialysis, medication and diet, specifically, related to the results.
Neither participant mentioned what Ms C might have wanted to communicate.

The participants' assessment

Both believed that the communication had, to some extent, been effective. Ms C said: *I could see it all clearly .....I didn't have any misunderstanding.*
However, through analysis of the video with each participant and with further discussion, evidence of extensive miscommunication emerged. The nurse had emphasised, during the interaction, that Ms C's haemoglobin level was low and had discussed its significance in terms of her health and the use of erythropoietin. In the exit interview, Ms C indicated that she believed that all her results were normal.

Sr D had discussed results of biochemical tests and the use of specific medications. She said: The patient knows a lot about medication and dialysis treatment .....she knows what medication she's on.
However, at exit interview, it became clear that Ms C had not understood key issues related to the results, that she was unable to name most of her medications, and that her understanding of their actions was completely different from the biomedical explanations she was given. The absence of shared understanding of key concepts related to results and medications was seen as an important source of miscommunication.

Consequences for clinical management

Both participants had perceived the communication to be effective. The discrepancy between perception and reality became evident only through triangulation of the data. Standard assessments of quality of care by the measurement of staff and patient satisfaction, in this case relating to education and staff-patient interaction, would not have revealed the miscommunication. This has important implications for clinical management. Best outcomes in the management of ESRD require adherence to a complex treatment regimen of regular dialysis, repeated tests, dietary restriction and daily medications.

CHAPTER 8: RENAL TRANSPLANTATION FOR INDIGENOUS AUSTRALIANS: IDENTIFYING THE BARRIERS TO EQUITABLE ACCESS.

Publication details:

Cass A, Cunningham J, Snelling P, Wang Z, Hoy W. Renal transplantation for Indigenous Australians: Identifying the barriers to equitable access. Submitted May 2002 *Ethnicity and Health.*

8.1: **Abstract**

Objective: To assess Indigenous Australians' access to renal transplantation, compared with non-Indigenous Australians. To examine whether disparities are due to a lower rate of acceptance onto the waiting list and/or a lower rate of moving from the list to transplantation.

Design: Retrospective national cohort study using data from the Australian and New Zealand Dialysis and Transplant Registry. We included all end-stage renal disease (ESRD) patients less than 65 years of age who started treatment in Australia between January 1993 and December 1998. We used survival analysis to examine the time from commencement of renal replacement therapy (RRT) to transplantation. We measured time from commencement of RRT to acceptance onto the waiting list (stage 1), and time from acceptance onto the waiting list to transplantation (stage 2). The main outcome measures were (1) acceptance onto the waiting list and (2) receipt of a transplant, before 31st March 2000.

Results: Indigenous patients had a lower transplantation rate (adjusted Indigenous:non-Indigenous rate ratio 0.32, 95% CI 0.25–0.40). They had both a lower rate of acceptance onto the waiting list (adjusted rate ratio 0.50, 95% CI 0.44–0.57) and a lower rate of moving from the list to transplantation (adjusted rate ratio 0.50, 95% CI 0.38–0.65). The disparities were not explained by differences in age, sex, co-morbidities or cause of renal disease.

Conclusions: Indigenous Australians face barriers to acceptance onto the waiting list and to moving from the list to transplantation. Further research to identify the causes could facilitate strategies to improve equity in transplantation.

8.2: Introduction

Indigenous Australians constitute less than 2% of the population, but over 10% of patients commencing treatment for end-stage renal disease (ESRD).[25] Between 1990 and 2000, the number being treated with dialysis or transplantation increased 230%. By contrast, the number of treated non-Indigenous Australians increased 78%.[104] In the year 2000, 17% of Indigenous patients had a functioning transplant. However, 47% of non-Indigenous patients had a functioning transplant.[104] The reasons for this disparity are ill-understood.

Transplantation is the optimal treatment for most patients with ESRD.[105] Compared with long-term dialysis, it confers better quality of life,[106] longer life expectancy[107] and significantly lowers costs.[105,108]

To receive a transplant, a new patient must negotiate the following steps:[109]

- being deemed medically suitable,
- Receiving appropriate education and giving consent,
- completing a transplant work-up,
- being accepted onto the waiting list and
- moving from the list to receive a transplant.

African-Americans are more likely than white Americans to remain stationary at each step.[110] No comparable information is available about Indigenous Australians, but the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA) has information on the time of starting dialysis, the time of being wait-listed, and the time of transplantation. We used these data to determine whether or not there are racial disparities, and, if so, whether they result from a lower rate of being wait-listed, from a lower rate of receiving a transplant, or from a combination of the two.

8.3: Methods

Database

ANZDATA maintains a data-base of all patients treated by maintenance dialysis or renal transplantation in Australia.[25] All renal units participate in the Registry. Survey forms are completed six-monthly for all patients until the date of death. The only patients not registered are the few who die before entering a dialysis or transplant program.

Patient data sets

Between 1 January 1993 and 31 December 1998, 8,128 patients commenced renal replacement therapy (RRT). We excluded data on 2,806 (34.5%) patients aged 65 years or over, who comprised less than 2% of all transplants. We therefore analysed data for 5,322 ESRD patients.

Variables

Outcomes were (1) acceptance onto the waiting list and (2) receipt of a transplant, before 31 March 2000. The Registry data include the date of commencing RRT, age, sex, primary renal disease, the presence of selected co-morbidities, Indigenous status, the six-month period in which the patient was first recorded as being on the waiting list and the date of receipt of their first transplant (if any). ANZDATA does not record the actual date of wait-listing. Co-morbid illnesses noted include diabetes, ischaemic heart disease, cerebrovascular disease, peripheral vascular disease and chronic lung disease.

Statistical analysis

Statistical analysis was performed using Stata software (Stata, version 7.0, College Station, Texas, 2000). We calculated:
the time to transplant from the date of commencement of RRT. This comprises two stages:

stage 1, the time to being wait-listed: from the date of commencement of RRT to the first day of the six-month period when first recorded as being wait-listed; and

stage 2, the time from being wait-listed to receipt of a transplant: the time from the first day of the six-month period when first recorded as being wait-listed to the date of transplant.

Patients were followed up until either receipt of a transplant, loss to follow up, or death.

We calculated the time to transplantation for the 5,322 patients. Because data pertaining to 16 (0.3%) patients' being wait-listed were missing, we excluded them from the stage 1 and stage 2 analyses.

Among the remaining 5,306 patients, 3,241 (61.1%) were wait-listed. As our aim was to explore the effect on equity of the cadaveric organ allocation guidelines, we excluded data on 600 patients who received a living donor transplant, leaving 2,641 patients for stage 2 analysis. Indigenous patients were significantly less likely to receive a living donor transplant (7.7% vs. 19.4%, $p<0.001$).

We calculated a transplant rate (transplants per 100 patient-years) for Indigenous and non-Indigenous patients. We used the Cox proportional hazards model to calculate Indigenous:non-Indigenous rate ratios for transplantation, stage 1 and stage 2. We adjusted for age, sex, co-morbidities and the cause of renal disease. We used the log rank test to compare Kaplan-Meier curves.

Ethical approval

We obtained approval from ANZDATA and the Joint Institutional Ethics Committee of the Royal Darwin Hospital and the Menzies School of Health Research.

8.4: Results

Of the 5,322 patients in the study, 663 (12.5%) were Indigenous (Table 8.1). Despite there being proportionately fewer Indigenous children, the median age of Indigenous patients was younger. Indigenous patients were more likely to be female, to have more comorbidities and to have had diabetes as their primary renal disease (Table 8.1).

Indigenous patients were significantly less likely to receive a transplant (11.8% v 38.6%; $p < 0.001$) (also see Table 8.2). Indigenous patients received 4.6 (95% CI 3.7–5.7) transplants per 100 patient-years, whereas non-Indigenous patients received 16.5 (95% CI 15.7–17.2). Kaplan-Meier curves, according to Indigenous status, indicate this difference graphically (p value for log rank test < 0.001) (Figure 8.1).

Indigenous patients were significantly less likely to be wait-listed (35.3% v 64.9%; $p < 0.001$) (also see Table 8.2). Kaplan-Meier curves clearly indicate this difference (p value for log rank test < 0.001) (Figure 8.2).

Of the 2,641 patients wait-listed for a cadaveric kidney, Indigenous patients were less likely to receive a transplant (27.4% v 49.5%; $p < 0.001$) (also see Table 8.2). Again, Kaplan-Meier curves indicate this difference according to Indigenous status (p value for log rank test < 0.001) (Figure 8.3).

Because exact date of wait-listing was not available, we performed sensitivity analyses, shifting the date within the six-month period in which a patient was first recorded as being wait-listed. Regardless of which date we used– the beginning, middle or end of the relevant six-month period–we still found markedly reduced access for Indigenous patients at each step.

8.5: Discussion

Our results indicate that Indigenous Australians are less likely to receive a transplant than are non-Indigenous Australians. We have identified barriers at being wait-listed and in moving from the waiting list to receiving a transplant. These disparities are not explained by differences in age, sex, co-morbidities or the cause of renal disease.

The quality of the data has some potential to affect the validity of our findings. First, although we adjusted our analysis for the *number* of co-morbidities, we believe that *severity* might be a better indicator of medical suitability for transplantation. ANZDATA does not collect data on severity. However, other research using this data set has shown that the number of co-morbidities is, itself, a significant indicator of health status and a strong predictor of mortality on RRT.[111] Even among patients who *were* wait-listed, Indigenous patients were significantly less likely to receive transplants. Second, the accuracy of Indigenous identification is a potential concern. We believe, however, that this is high, because of the ongoing, intensive interaction of patients with medical and nursing staff, the strong awareness of Indigenous ESRD among nephrologists, and Indigenous status being a prominent question in the six-monthly ANZDATA survey form.[24]

US research has shown that transplantation is associated with reduced mortality compared with wait-listed patients who do not receive a transplant, regardless of age or race.[107] Earlier Australian research had indicated poor patient and graft outcomes for Indigenous recipients.[11] However, a study of all transplants performed in Australia during 1993 to 1998 showed that Indigenous status was not now a significant predictor of graft survival at 12 months.[112] Recent research has confirmed that transplantation is associated with reduced Indigenous mortality.[113] If death rates can be significantly reduced by transplantation, there is a need to identify the reasons for an Indigenous patient being less likely than a non-Indigenous counterpart to receive a kidney.

The first barrier which we can identify from the available data lies between commencing dialysis and being wait-listed. Recent overseas evidence suggests that disparities in access to transplantation are not accounted for by differences in medical suitability or by patient preferences.[114,115] A survey of US nephrologists' reported attitudes to renal transplantation suggested that consideration of a patient's race might not be an explicit factor in the initial decision regarding medical suitability for transplantation,[116] but other studies suggest differences in actual practice. One study showed that, despite a subsequent assessment (using criteria developed by an expert panel), which demonstrated appropriateness for transplantation, African-Americans were significantly less likely than white Americans to have been referred for transplant evaluation or to have been wait-listed.[117] Of those patients deemed suitable and wishing to receive a transplant, African-Americans were less likely to complete a pre-transplant work-up, and were, therefore, less likely to be wait-listed.[109,117]

Recent Australian research, highlighting disparities in diagnostic and therapeutic procedures among Australian hospital patients identified as Indigenous, discussed the potential for discrimination that exists at multiple points within the healthcare system.[118] This should be considered when addressing inequities in access to renal transplantation. In Australia, almost 50% of Indigenous patients come from remote regions lacking ESRD treatment services.[24] Many who receive dialysis in rural or remote centres with small populations may well face significant practical impediments to completing a pre-transplant work-up, especially the non-availability of specialist services, such as coronary angiography.

One possible barrier on the way to the waiting list is informed patient consent, following education.[109] The content of educational resources, and the nature and quality of the communication between the patient and the relevant health-professional, are key factors.[119,120] Differences of language, ethnicity/culture and lifestyle,[121,122] as well as differences in literacy levels and health status,[123]

reduce the efficacy of education. In the case of Indigenous Australians, each of these factors may come into play. Low levels of patient understanding of both their renal disease and its treatments have also been linked to reduced active engagement of patients in their own long-term management.[16]

The second barrier revealed by our ANZDATA analysis lay between the waiting list and receipt of a transplant. Among African-Americans, this relates to a lower likelihood of identifying a living donor, and to a greater likelihood of blood type incompatibility and HLA (human leucocyte antigen) differences, both of which discourage 'inter-racial' transplantation.[124] In Australia, kidney allocation and distribution is managed according to the National Kidney Matching Scheme. The system is underpinned by potentially conflicting principles: the outcomes of kidney transplantation should be maximised *and* distribution should be equitable.[125] Although guidelines differ from state to state, HLA matching criteria are weighted more heavily than is waiting time.[125,126] As HLA antigens are distributed differently in different populations, and as most donor kidneys come from majority racial/ethnic groups, allocation based on HLA matching effectively discriminates against racial/ethnic minorities.[8,124,127]

While the use of kidneys with no HLA mismatches is associated with superior outcomes, completely matched kidneys account for only a small proportion of kidneys supplied through the cadaveric organ pool.[128] Advances in clinical transplantation have significantly reduced the effect of mismatching on graft survival.[124,129] Determining the allocation of the vast majority of cadaveric kidneys which are *not* perfectly matched is a proper area for debate on balancing quality of outcomes against equity of access.

Longer time on dialysis while awaiting transplantation, as currently experienced by most Indigenous Australians, is an independent predictor of worse 12-month graft survival.[112] In the US, the New England Organ Bank recently introduced allocation guidelines which make waiting time a much more significant determinant of ranking. This has resulted in improved access

for minority groups without outcomes being significantly compromised.[130] Similar alterations in allocation guidelines in Australia could increase access to transplantation for Indigenous Australians.

Being limited to the use of routinely collected national registry data, we could not address all five stages to transplantation. We cannot yet identify the most significant barriers facing Indigenous Australians. Further research into these areas could not only inform policy development on the improvement of equity in transplantation, but could also be relevant to improving equity of access to effective interventions for other chronic diseases affecting Indigenous Australians.

Table 8.1: **Patient characteristics at start of renal replacement therapy***

	Non-Indigenous (n=4659)	Indigenous (n=663)
Age (y)		
Median	49.5	47.0
Inter-quartile range	36.4 - 58.1	39.0 - 54.3
Sex, female	1930 (41.4)	372 (56.1)
Co-morbidities†		
Ischaemic heart disease	1196 (25.7)	209 (31.7)
Cerebrovascular disease	431 (9.3)	68 (10.3)
Peripheral vascular disease	886 (18.6)	137 (20.7)
Chronic airways disease	518 (11.1)	100 (15.1)
Diabetes mellitus	1098 (23.6)	437 (66.0)
Number of co-morbidities		
0	2592 (55.7)	164 (24.9)
1	914 (19.7)	219 (33.2)
2	536 (11.5)	149 (22.6)
3	353 (7.6)	87 (13.2)
4	218 (4.7)	35 (5.3)
5	37 (0.8)	6 (0.9)
Primary renal disease		
Primary glomerulonephritis	1842 (39.5)	197 (29.7)
Diabetes mellitus	878 (18.9)	299 (45.1)
Hypertension	236 (5.1)	33 (5.0)
Polycystic disease	420 (9.0)	5 (0.8)
Analgesic nephropathy	234 (5.0)	7 (1.1)
Reflux nephropathy	358 (7.7)	13 (2.0)
Other diagnoses	526 (11.3)	23 (3.5)
Uncertain	165 (3.5)	86 (13.0)

*Values listed as number (%) unless otherwise noted.

†Co-morbid illness categories are not mutually exclusive.

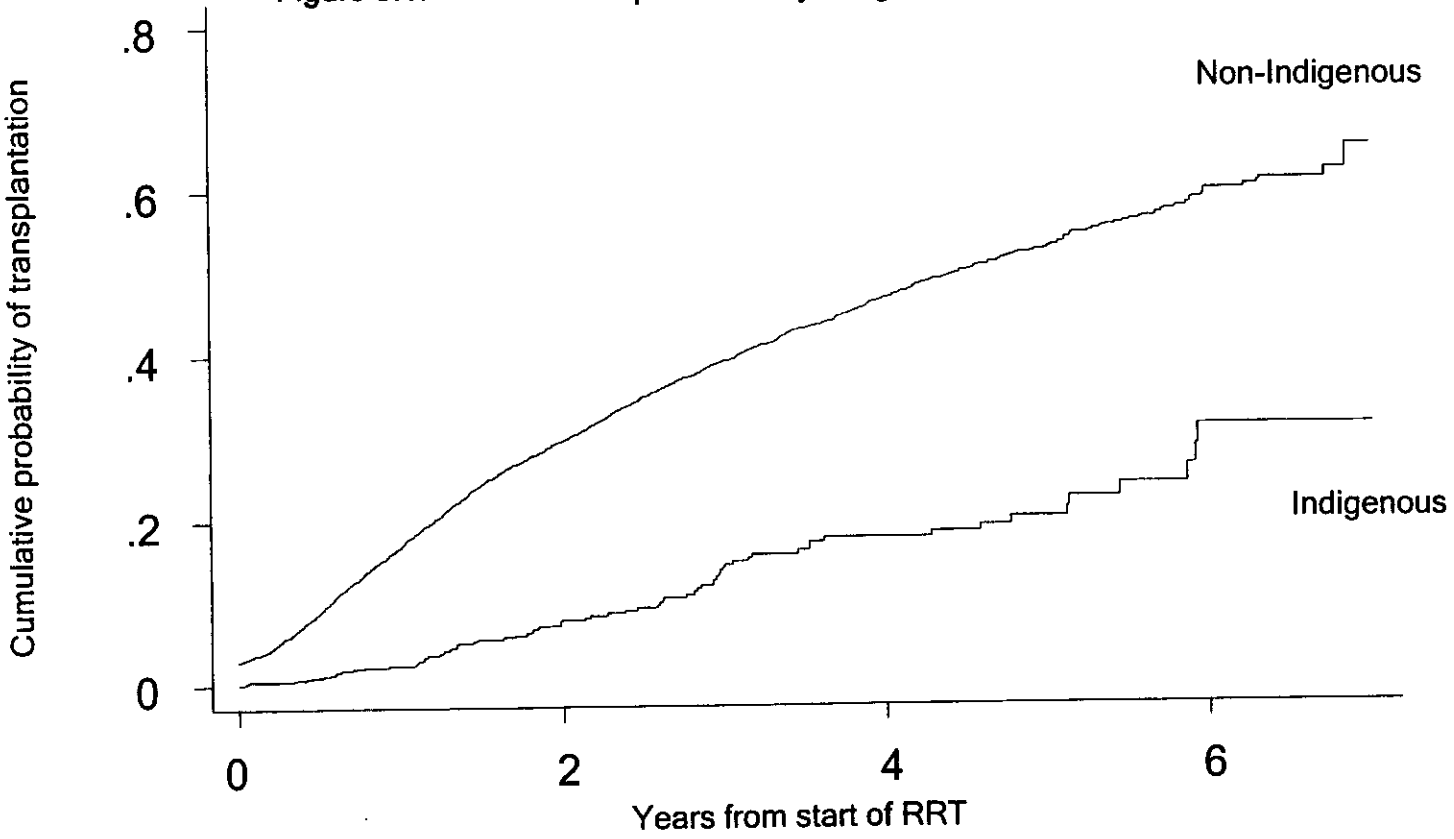
Table 8.2: Indigenous:non-Indigenous rate ratios for transplantation, by stages.

	Time to transplant (n = 5,322)	Stage 1* (n = 5,306)	Stage 2† (n = 2,645)
Crude rate ratio (95% CI)	0.28 (0.22–0.35)	0.44 (0.39–0.50)	0.48 (0.37–0.62)
Adjusted rate ratio (95% CI)	0.32 (0.25–0.40)	0.50 (0.44–0.57)	0.50 (0.38–0.65)

*Stage 1 defined as the time from the date of commencement of RRT to the first day of the six-month period in which the patient was first placed on the waiting list.

†Stage 2 defined as the time from the first day of the six-month period in which the patient was first placed on waiting list to the date of transplant.

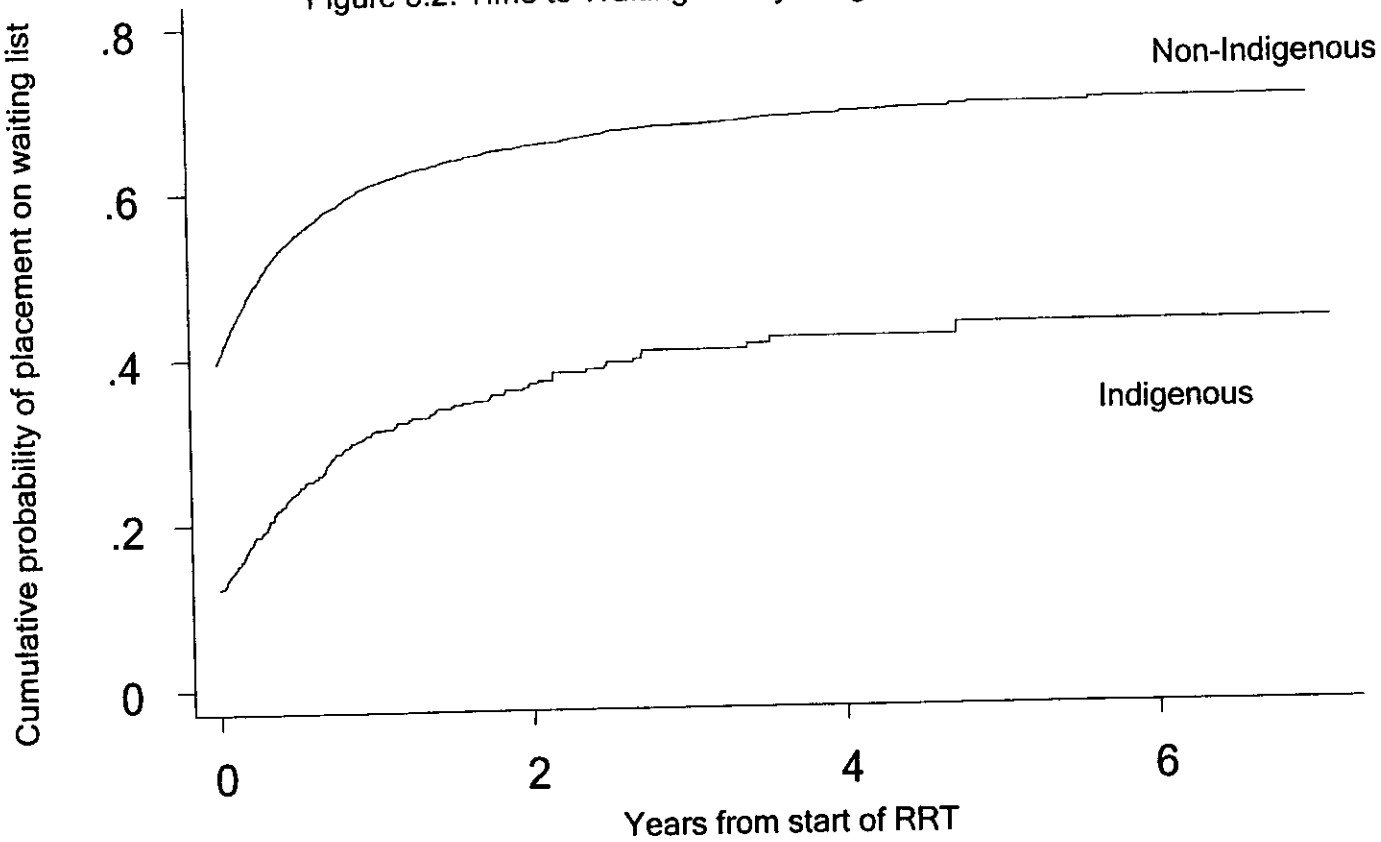
Figure 8.1: Time to Transplantation by Indigenous status



Number of patients at risk at beginning of specified year of study

	Year 0	Year 2	Year 4	Year 6
Non-Indigenous	4,659	2,345	787	151
Indigenous	663	343	136	26

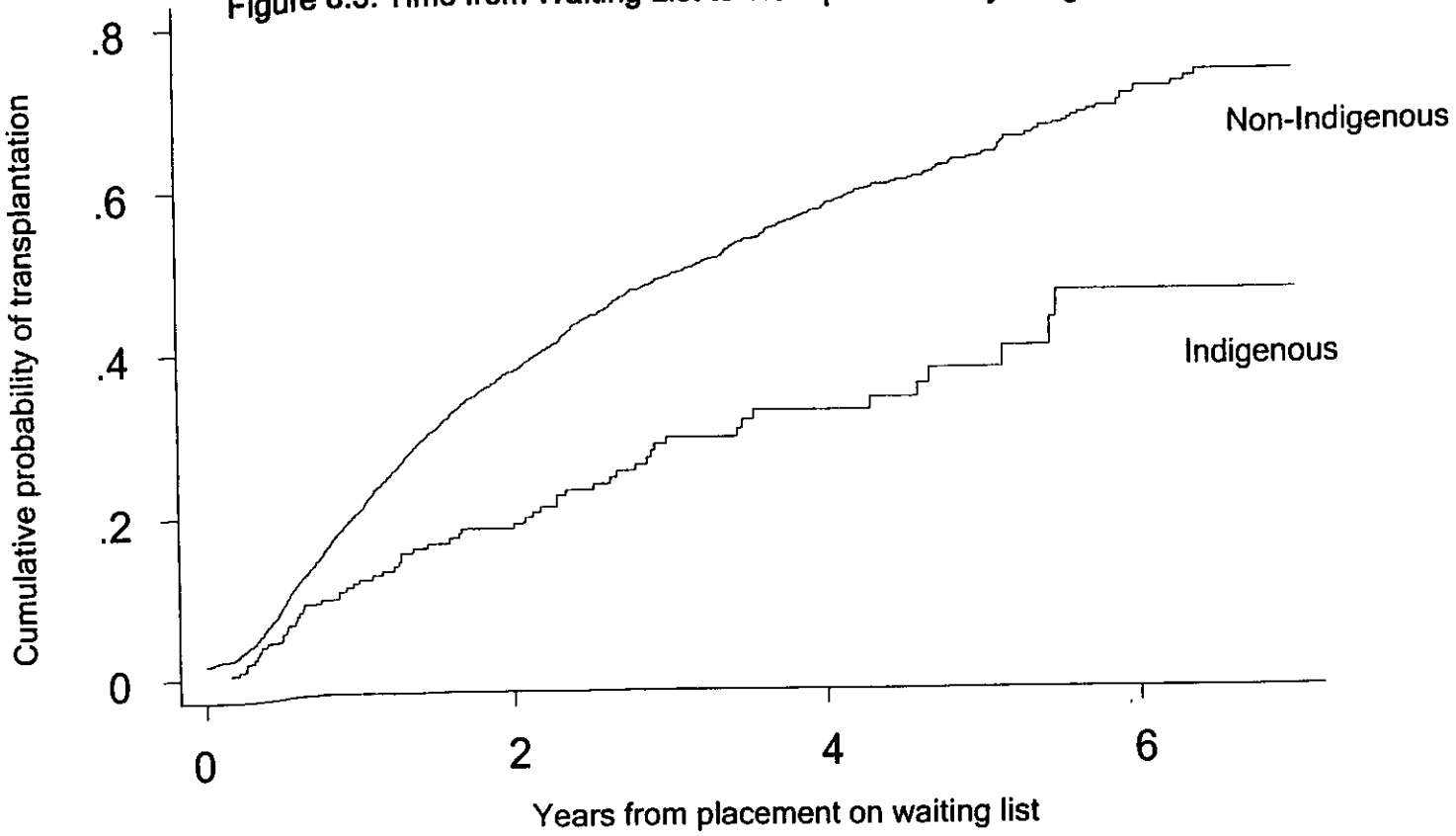
Figure 8.2: Time to Waiting List by Indigenous status



Number of patients at risk at beginning of specified year of study

	Year 0	Year 2	Year 4	Year 6
Non-Indigenous	4,644	937	279	61
Indigenous	662	232	67	15

Figure 8.3: Time from Waiting List to Transplantation by Indigenous status



Number of patients at risk at beginning of specified year of study

	Year 0	Year 2	Year 4	Year 6
Non-Indigenous	2,426	1,227	393	67
Indigenous	215	135	54	8

CHAPTER 9: CONCLUSION: EXPLORING THE PATHWAYS LEADING FROM DISADVANTAGE TO END-STAGE RENAL DISEASE FOR INDIGENOUS AUSTRALIANS

Publication details:

Cass A, Cunningham J, Snelling P, Wang Z, Hoy W. Exploring the pathways from disadvantage to end-stage renal disease. Submitted August 2002 *Social Science and Medicine*.

9.1: Abstract

Indigenous Australians are disadvantaged, relative to other Australians, over a range of socio-economic and health measures. The age- and sex- adjusted incidence of end-stage renal disease (ESRD), the irreversible pre-terminal phase of chronic renal failure, is almost nine times higher amongst Indigenous than it is amongst non-Indigenous Australians. A striking gradient exists from urban to remote regions, where the standardized ESRD incidence is from 20 to more than 30 times the national incidence. We discuss the profound impact of renal disease on indigenous people and communities. We explore the linkages between disadvantage and geographical location and the initiation of renal disease and its progression to ESRD.

Explanations for the excess burden of renal disease in indigenous populations can be categorised as: 1) the primary renal disease explanation; 2) the genetic explanation; 3) the early development explanation; and 4) the socio-economic explanation. We discuss the strengths and weaknesses of these explanations and propose a new model which integrates the existing evidence. We use this model to illuminate the pathways between disadvantage and the human biological processes which culminate in ESRD, and to propose prevention strategies across the life-course of Indigenous Australians to reduce their ESRD risk.

The model we have developed is likely to be relevant to an understanding of patterns of renal disease in other high-risk populations. Furthermore, similar pathways might be relevant to other chronic diseases, such as diabetes and cardiovascular disease, among indigenous populations throughout the developed world and to the populations of developing countries. As we are able to confirm the many pathways from disadvantage to human biology, we are better placed to advocate evidence-based interventions, both within and beyond the scope of the healthcare system, in order to address the excess burden of renal and other chronic diseases among Indigenous Australians and other affected populations.

9.2: Introduction

On November 11th 2000, Sotheby's held an auction of Australian Aboriginal artworks at the Art Gallery of New South Wales, in Sydney. Thirty-five pieces of art were auctioned, including a number of canvases painted by residents of Kintore and Kiwirrkura, two remote Aboriginal communities hundreds of kilometres west of Alice Springs in Central Australia. The auction was part of the Western Desert Dialysis Art Appeal, which raised over one million Australian dollars. Why would two remote Aboriginal communities, each with only a few hundred residents, need a haemodialysis unit?

Haemodialysis is used to treat end-stage renal disease (ESRD), the irreversible pre-terminal phase of chronic renal failure. A person suffering ESRD will die without treatment. In the developed world, treatment for ESRD is generally available, either in the form of maintenance dialysis (the majority of which is haemodialysis) or renal transplantation. Haemodialysis is an expensive tertiary care service, usually provided in urban centres only. Aboriginal Australians with ESRD in remote communities such as Kintore and Kiwirrkura must leave their community to commence dialysis. Very few receive transplants; most remain on haemodialysis, hundreds of kilometres from home, in a satellite unit of an urban hospital. The people of Kintore and Kiwirrkura have taken drastic action to keep sick members in the community. But why are these communities so affected by ESRD in the first place, when fewer than 1 in 10,000 Australians start ESRD treatment each year?[131]

As a group, Indigenous Australians (Aborigines and Torres Strait Islanders) are disadvantaged, relative to other Australians, over a range of socio-economic and health measures. In 1996, Indigenous adults were less likely to have a post-school educational qualification (11% v 31%), more likely to be unemployed (23% v 9%), and much less likely to own or to be purchasing their home (31% v 71%).[23] The median weekly income for Indigenous males was $189, compared with $415 for non-Indigenous males. The disparity between

females was not as marked, with median weekly income of $190 and $224 respectively.[23]

In 1997-1999, estimated life expectancy at birth of Indigenous Australians was 56 years for males, compared with 76 for all males, and 63 years for females, compared with 82 for all females.[132] Most of the difference is due to premature adult mortality from chronic diseases,[133] many of which are related to ESRD.

The incidence of ESRD throughout the developed world is markedly higher amongst indigenous people.[108,131,134] During the 1990s, the crude incidence of ESRD in Indigenous Australians more than doubled.[131] In 2000, Indigenous Australians constituted less than 2% of the national population, but over 8% of new patients commencing treatment for ESRD.[131] ESRD is generally a disease of older people. However, the Australian Indigenous population is much younger than the general population, with a median age in 1996 of 20 years, compared to 34 years for the total Australian population.[132] Crude ESRD figures, therefore, understate the difference between the Indigenous and non-Indigenous populations. After adjusting for age and sex, the ESRD incidence rate in 1997 was almost nine times higher for Indigenous Australians than for non-Indigenous Australians.[10]

The burden of ESRD is greater everywhere for Indigenous Australians but there are striking geographical differences in the incidence of ESRD within the Indigenous population (Figure 3.1). A large gradient exists from urban to remote regions.[135] In remote communities, including places like Kintore and Kiwirrkura, the standardized ESRD incidence is from 20 to more than 30 times the national incidence (Figure 3.1). Can we explain the link between disadvantage and geographical location on the one hand, and the initiation of renal disease and its progression to ESRD on the other?

Several explanations have been offered for the excess burden of renal disease in Indigenous populations and in other minorities, for example, African Americans. These explanations can be categorised as:

1) the primary renal disease explanation: population differences result from a higher incidence, and greater severity, of primary diseases which cause ESRD;
2) the genetic explanation: genetic differences determine patterns of ESRD;
3) the early development explanation: an adverse intra-uterine environment affects kidney development leading to a vulnerability to ESRD and;
4) the socio-economic disadvantage explanation: greater socio-economic disadvantage in minority and Indigenous populations results in a higher incidence of ESRD.

As we will demonstrate, each of these categories of explanations have strengths and weaknesses and they are not mutually exclusive. We propose a new model which integrates the existing evidence. We then use the model to illuminate the pathways between disadvantage and the human biological processes which culminate in ESRD, and to propose prevention strategies across the life-course of Indigenous Australians to reduce their risk of ESRD.

9.3: The primary renal disease explanation

Nephrologists conceive of the causes of ESRD in terms of primary renal diseases which cause kidney tissue damage, resulting eventually in ESRD. In the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA), which covers all Australian renal units, cases are assigned to one of 69 primary renal diseases.[131] Examples include membranous glomerulonephritis, analgesic nephropathy, renal vascular disease due to hypertension, polycystic kidney disease and type 2 diabetes. The diagnostic criteria are not mutually exclusive and the boundaries between the various disease entities are not clearly defined.[136] However, in order to facilitate discussion of the distribution of causes of ESRD, the 69 primary renal diseases may be classified according to eight major diagnostic categories (see Table 9.1).[131]

Among new ESRD cases in Australia during 1993 to 1998, there were different patterns of primary renal disease, according to whether or not the patient was Indigenous (Table 9.1). Almost half of ESRD cases in Indigenous Australians were attributed to diabetes, compared to approximately one in six non-Indigenous cases. Glomerulonephritis was attributed as the cause of more than one in four Indigenous patients and approximately one in three non-Indigenous patients. Indigenous patients were significantly more likely to have an uncertain diagnosis recorded. Other disease categories were less common among the Indigenous than the non-Indigenous (Table 9.1).

The validity of the attribution of ESRD to primary causes has been questioned.[136] Disparities in classification of primary renal diseases hinder cross-national comparisons of the frequency of primary renal diseases leading to ESRD.[26] Because histopathological examination of renal tissue obtained at percutaneous biopsy has been considered the diagnostic gold standard, it could be argued that increased use of renal biopsy might improve the accuracy of diagnosis of the causes of ESRD. However, there is evidence that even the interpretation of histological findings is affected by the nephrologist's knowledge of the patient's 'race'.[136]

For example, nephrologists in a US study were sent written case histories based on the presentation of seven ESRD patients. The patient's race was randomly allocated to be 'black' or 'white'. When the race of the patient was specified as 'black' rather than 'white', the same case history of renal failure was almost twice as likely to be diagnosed as ESRD due to hypertension.[137] Similarly, Indigenous Australian ESRD patients, who are more likely than non-Indigenous patients to have diabetes at the time of commencement of treatment (66% v 24%, $p<0.001$), may be more likely to have their ESRD attributed to diabetes, whether it is the fundamental cause of renal damage or merely a coincidental illness.

Since 1998, ANZDATA has collected data recording whether or not new ESRD patients have a diagnostic renal biopsy. During 1998 to 2000, 37% of 5,115 new ESRD patients had a diagnosis based on renal biopsy (ANZDATA, special data request, 2002). Fewer Indigenous than non-Indigenous patients underwent biopsy (27% v 38%, $p<0.001$). This can be explained, at least in part, by a greater proportion of Indigenous ESRD patients presenting late in the course of their disease and by their much greater prevalence of diabetes.

A study of the consequences of late referral for care by a nephrologist showed that 39% of Indigenous ESRD patients needed to commence dialysis within three months of referral to a nephrologist (i.e. they were referred late) compared to 26% of non-Indigenous ESRD patients.[138] For patients near to needing dialysis, not only is the risk of significant complications with renal biopsy much greater,[139] but biopsy specimens are often uninformative, showing only non-specific evidence of scarring and atrophy.[136] Patients with their ESRD attributed to diabetes were less likely to have undergone biopsy (ANZDATA, special data request, 2002). Among the 45% of Indigenous cases attributed to diabetes, only 17% had a confirmatory biopsy, and among the 20% of non-Indigenous cases attributed to diabetes, only 19% had a confirmatory biopsy. Although intuitively appealing, the primary renal disease explanation adds little to our understanding of why Indigenous Australians

have a higher burden of ESRD. In practice, it offers an imperfect taxonomy rather than an explanation.

9.4: The genetic explanation

Many researchers propose that both the initiation of renal disease and its progression to ESRD are genetically determined.[140] Research examining the high ESRD incidence in ethnic minorities, including Indigenous minorities, has focused on 'racial' differences in physiological processes and pathological responses.[141] These responses have been attributed to genetic factors.[20,140,141]

There is substantial evidence that ESRD clusters in families.[142-144] This familial aggregation occurs in excess of that predicted by the clustering of risk factors, including the presence and severity of diabetes and hypertension.[145] Familial clustering of diabetic and non-diabetic renal disease has been reported among Pima[146] and Zuni Indians.[147] Familial clustering of proteinuria, a marker of renal disease, has also been demonstrated in a number of Indigenous Australian communities.[148,149] However, familial clustering might reflect shared exposure to adverse socio-economic or environmental factors, rather than a genetic predisposition.

Among Indigenous populations, high ESRD rates have been related to the growing epidemic of type 2 diabetes.[134,150] The 'thrifty genotype' hypothesis has been advanced as a possible explanation for the epidemic of type 2 diabetes in Indigenous populations as they make the rapid transition from traditional lifestyles to western diets and lifestyles.[151] Neel postulated that the 'feast and famine' conditions which prevailed throughout most of human history might have selected for a 'thrifty' metabolism, facilitating efficient fat storage in times of food abundance and providing an energy buffer in times of scarcity.[151] Using this hypothesis, the steep gradient in incidence of ESRD from urban to remote regions among Indigenous Australians[135] could be explained by 'genetic admixture': urban Indigenous Australians might be protected to some degree from type 2 diabetes, and therefore from ESRD, through several generations of non-Indigenous admixture.[152]

The 'thrifty genotype' hypothesis has subsequently been questioned, not least by its original proponent. Neel recently suggested that his original hypothesis had presented an overly simplistic view of the physiological adjustments involved in the transition from a hunter-gatherer lifestyle to a western lifestyle.[153] He reviewed evidence relating to the high incidence of type 2 diabetes among American Indians and concluded that it must predominantly reflect environmental changes rather than a 'racial' or genetic predisposition.[153] Similarly, the rapidity of the increase in ESRD incidence among Indigenous Australians over the last 25 years[11] is not compatible with a genetic explanation.

Nevertheless, as with other chronic diseases, genes are not irrelevant, and differences in susceptibility, possibly attributable to genetic differences, are of interest. Genetic studies have reported possible locations of 'renal failure susceptibility genes' in Indigenous populations.[150] Two strategies have been widely used in searches for genetic linkage.[143] The first, a 'candidate gene' approach, analyses the relationship between the disease of interest and the presence of a polymorphic DNA marker within or near a possible causative gene. One limitation with this approach is that it is constrained to testing for known genes.

In nephrology, this line of research has focused predominantly on genes coding for the renin-angiotensin system, which plays a central role in blood pressure regulation.[150] It has been postulated that, in Caucasians, the DD genotype of the ACE gene is an independent risk factor for renal disease,[154] associated with an increased rate of progression of kidney damage in diabetes[155,156] and IgA glomerulonephritis.[157] However, others have failed to replicate these associations.[158,159] The DD genotype of the ACE gene occurs infrequently in Indigenous Australians,[160] in whom no significant influence on renal disease has been demonstrated. A recent study in a remote Indigenous Australian community has, however, found an association between a common polymorphism of the p53 gene and proteinuria.[161]

The second approach to genetic linkage studies, involving a genome-wide search, has the potential to locate previously unknown genes which might contribute to disease. In this strategy, hundreds of highly polymorphic micro-satellite markers, which provide complete coverage of the human genome, are tested for co-inheritance with the disease.[143] For diseases demonstrating late age-at-onset, such as ESRD, affected sibling pairs are commonly used to evaluate evidence of genetic linkage.[143] This is because few ESRD patients will have living parents, and the children of the affected individuals might be too young to demonstrate even early markers of renal disease.

Imperatore et al. undertook a genome-wide scan for loci linked to diabetic nephropathy among 98 diabetic Pima Indian sib-pairs.[162] They found four chromosomal areas with possible linkage to diabetic nephropathy. The strongest evidence for linkage was on chromosome 7. The peak LOD score (an indicator of the strength of linkage between the genetic locus and disease phenotype under investigation) for the area on chromosome 7 did not reach the threshold for statistical significance in a genome-wide scan.[162] The evidence for linkage for three other regions on chromosomes 3, 9 and 20 was suggestive, but again not statistically significant.[162] Among Indigenous Australians, a genome-wide scan for susceptibility to type 2 diabetes reported linkage to an area on chromosome 2,[163] but this methodology has not been used to examine renal disease susceptibility in Indigenous Australians.

Explanatory models for disease which give primacy to genetic determinants focus almost exclusively on individual biological and behavioural correlates of illness.[164] However, in disorders of multifactorial origin, including ESRD, where environmental and socioeconomic factors influence health status, gene/gene and gene/environment interactions are complex.[165] Much of the genetic research has been based on 'racial difference', a concept which lacks a firm scientific foundation.[166] The American Association of Physical Anthropology has concluded, "pure races in the sense of genetically homogeneous populations do not exist in the human species today".[167] By contrast with the considerable biological variation *within* human populations,

the biological differences *between* population groups are small. These differences reflect both inheritance and the influence of the natural and social environment, with most differences being attributed to their interaction.[166] Genetic approaches to understanding Indigenous ESRD tend to ignore a large and growing body of literature emphasizing the primacy of social, cultural and environmental factors in determining patterns of disease in particular populations.[164]

9.5: The early development explanation

Early development provides a good example of the nexus between genes and the environment, and of the difficulty in separating them. There has been much interest recently in the relationship between foetal and/or infant growth and nutrition and adult chronic disease.[168-170] Foetal malnutrition, marked by low birth weight (LBW), has been linked with a predisposition to hypertension, type 2 diabetes, dyslipidaemia and cardiovascular disease.[171-173] Intrauterine malnutrition has also been linked with the progression of renal injury[174] and a predisposition to ESRD among Indigenous Australians.[21] The uterine environment is potentially relevant to ESRD because of the development of the kidneys during intrauterine life.

Nephrons, the functional units of the kidney, begin to form around week 8 of gestation,[175] but the majority form in the third trimester.[176] None develop after birth.[175,177] The number in a whole kidney can be reliably estimated using direct stereological counting.[178] Evidence from autopsy studies suggests a wide range in the number of nephrons in the "normal" kidney.[179] Nephrons are lost both with ageing[179-181] and due to a variety of nephropathic insults. Damage to the glomerulus, the filtration segment of the nephron, is marked by protein leakage into the urine, making the appearance of urinary protein or albumin a marker of early renal disease.

Although the number of nephrons is fixed at birth, glomerular size can increase in response to a deficit in numbers,[175] with a resulting restoration of total filtration surface and excretory homeostasis. However, this adaptation might come at a high price. The excessive glomerular enlargement might accelerate the loss of nephrons through glomerular hypertension and hyperfiltration injury.[182] Increased glomerular capillary pressure has been postulated as a key mediator of progressive scarring (sclerosis).[183] This scarring induces a self-perpetuating cycle of nephron loss leading to further enlargement, increased flow and pressure in the remaining glomeruli, leading to further sclerosis and nephron loss. This process might culminate in ESRD

with insufficient nephrons to sustain life. It seems plausible that people born with fewer nephrons might be predisposed to develop hypertension, progressive renal insufficiency and ESRD.[174,184] They might, in effect, have less renal reserve to lose.

Intrauterine[175,177] and/or genetic influences[185,186] might determine nephron number. Intrauterine growth retardation (IUGR), usually defined as being within the lightest 10% of birth weights in a standard population in each gestational age stratum, is not a specific disease entity *per se*, but rather a manifestation of various foetal and maternal disorders.[187] Among Indigenous Australians, maternal malnutrition, smoking and teenage pregnancy have been established as important causes of IUGR.[188] In a 1987 to 1991 study in a large hospital, 114 (22.7%) of 502 Indigenous babies were recorded as having IUGR.[189] In 1994-1996, low birth weight (also a marker of foetal malnutrition) occurred in 12.4% of Indigenous births compared with 6.2% of non-Indigenous births.[32]

Merlet-Benichou and colleagues, using rat models of kidney development, have suggested that the foetal environment plays a determining role in kidney development.[190] Research has suggested that maternal malnutrition,[191] maternal hyperglycemia,[192] drug exposure[193] and vitamin A deficiency[194] impair kidney development and result in reduced nephron number in the offspring. In animal models, IUGR produced by partial uterine artery ligation leads to a permanent nephron deficit.[195] However, the relevance of such animal models to human renal development has been questioned.[196]

A small number of histological studies in humans have explored the association between nephron number and IUGR or birth weight. A retrospective study of 35 neonatal deaths[197] showed a strong correlation between glomerular number and birth weight ($r=0.87$, $p<0.0001$). IUGR was associated with a significant reduction in nephron number in a prospective study of 32 stillbirths and infant deaths.[177] In a study of 24 full-term infants who died in-utero or within 6 months of birth, nephron number was reduced by 30%

in those with IUGR.[198] A current autopsy study is examining the relationship between nephron number, size and birth weight in Australian Aborigines, African Americans and Caucasians.[199] A preliminary report indicates that children and adults with low birth weight (LBW) have, on average, 37% fewer nephrons than those with higher birth weights.[200]

There is also evidence of a relationship between birth weight and clinical or pathological evidence of progressive renal disease. IUGR or low birth weight has been associated with macroalbuminuria (albumin excretion more than 300mg per 24 hours) in type 1 diabetes,[201] with macroalbuminuria in Pima Indians with type 2 diabetes,[202] and with progression of disease in children with IgA nephropathy.[203] A retrospective study of adults born at the local maternity hospital in Preston, England, suggested an association between LBW and microalbuminuria (albumin excretion between 30 and 300 mg per 24 hours).[204] As only eleven of the 236 subjects (5%) had microalbuminuria, the study lacked the power to detect a significant difference in birth weight between the groups.

By contrast, high rates of albuminuria have been found in rural and remote Indigenous communities in Australia.[149,205,206] In one prospective cohort study, the level of albuminuria at screening predicted risk of death and progression to ESRD.[207] Birth weights were available from clinic records for the majority of the adults screened. After adjustment for age, gender, BMI and blood pressure, the odds ratio for macroalbuminuria in low birth weight persons, compared to those with higher birth weights, was 2.82 (95% CI 1.26 to 6.31).[21] There is evidence, therefore, among Indigenous Australians that birth weight is linked to albuminuria, which predicts progression to ESRD.

Published biopsy series from Indigenous Australians with overt renal disease show a wide range of morphological diagnoses.[208] Pathological changes in the glomerulus can usually be characterized by one or more of the following basic tissue reactions:[209] hypercellularity, basement membrane thickening, hyalinization and sclerosis. However glomerulomegaly, or glomerular

enlargement in the absence of hypercellularity, is a striking finding in kidney biopsies from Indigenous, but not from non-Indigenous Australians.[208,210,211] Glomerulomegaly has also been demonstrated in African Americans.[212,213] A current autopsy study, which includes Indigenous Australian, African American and Caucasian subjects, has demonstrated a significant inverse relationship between glomerular number and glomerular size.[199,214] These findings are consistent with the hypothesis that reduced nephron number at birth might confer an increased susceptibility to renal disease and that compensatory enlargement of remaining glomeruli might lead to progressive damage through glomerular hyperfiltration and scarring.

This substantial body of research suggests that nephron endowment at birth, crucially influenced by the intrauterine environment, might be causally related to the development of ESRD in adult life. However, foetal growth might not be linked causally to chronic disease. There might be shared genetic mechanisms for foetal growth and later chronic disease.[215] The validity of the suggested association between foetal development and chronic disease has also been questioned on the basis of a perceived failure to define, measure and adequately control for confounding due to socioeconomic disadvantage.[216]

9.6: The socioeconomic disadvantage explanation

There is strong evidence of a relationship between socioeconomic position and overall morbidity and mortality.[17] The gradient in the occurrence of disease progressively favours those of higher socioeconomic status.[18] This has been confirmed amongst Australians.[1,3,19] In general, research into Australian health inequalities has inadequately controlled for confounding by Indigenous status and has failed to investigate health gradients within the Indigenous population.

Inconsistent results have been obtained from the few previous studies of the association between socioeconomic status and the incidence of ESRD.[36-40] A study in the Grampian region of Scotland[37] found no association between socioeconomic status and the incidence of ESRD. In New York,[38] an association was found in White, but not in African Americans. In a nationwide US study,[39] a 60% higher incidence of ESRD was found in the lowest compared to highest income categories for both White and African Americans. In a study of ESRD incidence in Australian capital cities, we found a significant association between the incidence of ESRD and a regional level index of disadvantage,[36] with up to three-fold variation in incidence. An individual level, population-based, case-control study of patients starting ESRD treatment in four East Coast states in the US[40] found that the adjusted risk for development of ESRD was 4.5 times higher in the lowest compared to the highest income category, with a similar gradient for White and African Americans.

Only one study of social disadvantage and ESRD in Indigenous Australians has been reported to date.[135] In this ecological study, strong associations were evident between age- and sex-standardised, area-level, ESRD incidence (based on ANZDATA Registry information) and area-level markers of social disadvantage (Table 3.1). The correlation with the overall rank of socio-economic disadvantage was particularly strong (Table 3.1 and Figure 3.2). Although it has been argued that area-level measures of social disadvantage are poor surrogates for individual-level characteristics,[217] it is becoming

increasingly accepted that community-level exposures to features of the social and physical environment in which people live might directly affect health outcomes.[218] For example, in many disadvantaged Indigenous communities there is poor access to preventive health services and to stores selling healthy foods at reasonable prices, as well as a lack of community infrastructure for basic water, sewerage and housing needs.[219]

9.7: Towards an integrated model of Indigenous ESRD

How might disadvantage lead to ESRD? What pathways or mechanisms lead to the biological expression of Indigenous Australians' experiences of economic and social disadvantage, thereby producing the steep social gradient in the incidence of ESRD? How can we integrate our understanding of the suggested pathophysiological pathways to ESRD with what we know about the social determinants of health?

Chronic disease epidemiology has generally conceived risk of disease as residing within individuals and in their personal behaviour[220] and has therefore focused on proximate, individual-level risk factors.[221] The interactions among individuals and between individuals and their social and physical environment are either considered as potential confounders or fall completely outside the scope of most research.[220] However, individual-level risk factors do not completely explain social gradients in health. For example, in the original Whitehall study, a prospective cohort study of 17,530 male public servants in London, conventional individual-level risk factors for coronary artery disease– blood pressure, smoking, cholesterol, BMI and level of physical activity– explained only one quarter of the observed social gradient in coronary disease mortality.[222] In recognition of the shortcomings of the traditional approach, interest in what has come to be known as 'social epidemiology' has grown markedly in recent years.

Social epidemiology is concerned with the social distribution and social determinants of health and illness.[223] According to Krieger,[224] the three main theories invoked to explain social inequalities in health are: 1) psychosocial; 2) the social production of disease or the 'political economy' of health; and 3) ecosocial theory and related multi-level frameworks.

Psychosocial theories concentrate on endogenous biological responses to human interactions.[224] Chronic anxiety, insecurity, low self-esteem, social isolation and lack of control over work affect mental and physical health.[225]

Psychosocial stressors might be directly pathogenic,[224] affecting a range of physiological pathways, or they might affect health indirectly through stress-induced behaviours such as smoking. The physiological systems mediating biological responses include the autonomic nervous system, the hypothalamic-pituitary-adrenal (HPA) axis, and the cardiovascular, metabolic and immune systems.[226] Acute stress initiates adaptive, physiological responses involving the autonomic nervous system and the HPA axis, the 'fight or flight' response, but chronic and/or repeated stress might lead to maladaptive, pathological responses.[226]

The social production of disease theories propose, by contrast, that the fundamental causes of social inequalities in health are the actions of the economic and political institutions which create and perpetuate economic and social privilege and disadvantage.[224] Health inequalities result from the differential accumulation of exposures and experiences which originate in material disadvantage.[227] Health inequalities are rooted in the social structure, rather than in individuals' behaviour or in their inability to manage stress.[224]

An ecosocial theoretical framework integrates biological and social explanations for health inequalities by examining how we embody, or incorporate biologically, the material and social world in which we live.[224] The pathways linking disadvantage and disease are formed both by societal arrangements of power and property, and by the constraints and possibilities of our biology.[224] There is a cumulative interplay between exposure, susceptibility and resistance, with each factor and its contribution conceptualised at multiple levels–individual, community, regional, national and global.[224] Can we use an ecosocial framework to understand the ESRD burden in Indigenous populations? What evidence would enable us to outline discrete pathways linking disadvantage and biological processes, culminating in ESRD in Indigenous Australians?

9.8: Multi-level pathways linking experiences of disadvantage and their biological embodiment in ESRD in Indigenous Australians

In Figure 9.1, we propose an integrated model of ESRD in Indigenous Australians. This model is based on the work of Turrell and others,[19] but has been changed to make it more specific to ESRD. We will outline a number of direct and indirect pathways linking disadvantage and kidney disease. In the following section, we discuss the evidence, largely from research amongst Indigenous Australians, to support these pathways.

1) Direct linkage from disadvantage to renal damage

There is strong evidence linking house crowding, via endemic streptococcal skin infection, to the incidence of ESRD.[135] Living conditions, notably overcrowded sleeping arrangements, have been associated with the presence of scabies.[228-230] Scabies and streptococcal skin sores are the most important skin infections in central and northern Australia.[230] Scabies is endemic in many remote communities, being found in up to 50% of children. The cycles of scabies transmission underlie the high prevalence of skin sores. Up to 70% of children have skin sores, with group A streptococcus (GAS) being the major pathogen.[230,231]

In a cross-sectional study in a high-risk remote community, the presence of skin sores and scabies in both children and adults was associated with macroalbuminuria.[149] Adults with persistent antibodies to streptococcal M protein, markers of past GAS infection, were far more likely than those lacking such antibodies to have macroalbuminuria.[232] GAS is responsible for the continuing outbreaks of acute post-streptococcal glomerulonephritis (APSGN).[230,231,233] A retrospective cohort study showed that adults with a documented remote history (14.6 years earlier on average) of APSGN had an adjusted odds ratio of 6.1 (95% CI, 2.2–16.9) for macroalbuminuria, compared with adults lacking a history of APSGN. [234]

2) Indirect linkage via psychosocial factors

It has been proposed that biological responses to environmental stress could mediate the predisposition to poor health outcomes of Indigenous populations in industrialized countries.[235] In one study, glycosylated haemoglobin concentration, which is elevated by stress-associated catecholamine release, was measured as a biomarker of 'psychogenic stress'. An analysis of the data, controlled for diabetic status, found that glycosylated haemoglobin concentration was higher in Indigenous Australians.[235] We have demonstrated a strong association between high unemployment, low educational attainment, low income and the incidence of ESRD.[135] Stress, lack of control over one's life, social isolation and alienation are consequences of unemployment, poor education and low income.[223]

To some extent, the much steeper social gradient in the incidence of ESRD[135] might be due to the greater relative disadvantage of Indigenous Australians. However, aspects of colonisation and 'westernisation', including dispossession and separation from their land, forced removal of children from family and kin, racial discrimination and social marginalisation, have been recognised as key issues affecting health status.[236,237] Loss of control over their own lives, their communities and their environment has been identified as a potent cause of ill-health.[94]

Although a growing body of evidence associates chronic stress and psychosocial factors with a range of health outcomes relevant to the initiation and progression of renal disease, including hypertension,[238,239] progression of atherosclerosis[240] and susceptibility to infection,[241] research along these lines has not yet been undertaken amongst Indigenous Australians.

3) Indirect and inter-generational linkage via damaging health behaviours

Australians of lower socio-economic status are more likely to smoke, to be overweight and to be inactive.[3] Indigenous adults are even more likely to smoke and to be obese.[23] Nationally, approximately 54% of Indigenous

Australians smoke, compared with 22% of all Australians.[242] Smoking, obesity and lack of exercise are risk factors for diabetes, hypertension and hyperlipidaemia. These conditions might both initiate renal damage and facilitate progression of existing renal disease towards ESRD.[243,244]

Smoking is associated with albuminuria and abnormal renal function.[245] It is an established risk factor for ESRD,[82] and is associated with progression of renal disease.[246,247] Both active[248] and passive[249] smoking have been associated with endothelial dysfunction in human studies. Endothelial cell function might be crucial in determining whether healing or scarring will result after renal injury.[183] Normally, glomerular endothelial cells inhibit cellular processes which lead to scarring. However, in response to a variety of stimuli, which might include smoking, glomerular endothelial cells release endothelin[250] and plasminogen activator-inhibitor-1.[251] These factors have been linked, *in vitro*, to hypertrophy of the glomeruli, increased cellular matrix and fibrosis, processes which lead to renal scarring.[183]

Smoking might also play a role in the inter-generational transfer of risk for ESRD. Maternal malnutrition and smoking are known causes of IUGR.[188] IUGR is commoner among Indigenous births[32] and might result in lower nephron endowment and a predisposition to ESRD.

4) Indirect linkage via factors in the healthcare system

Socio-economic disadvantage, residence in remote communities and racial discrimination are associated with limited access to the health care which might otherwise prevent ESRD. For example, Indigenous women are less likely to attend antenatal care early in their pregnancy and are more likely to have two or fewer attendances.[252] This might relate to both socio-economic disadvantage[19] and to remoteness from antenatal services.[252] Late presentation to antenatal services has been associated with risk of low birth weight.[253] Almost 200 Indigenous communities, mostly in Northern and Central Australia, are more than 100 km from the nearest primary health care

facility.[219] In addition to antenatal services, primary health care provides a range of services which could prevent ESRD, such as scabies eradication programs.[254]

Remote Indigenous Australians also suffer from reduced access to secondary prevention programs which could reduce the risk of renal disease progression. There is evidence from numerous randomised controlled trials and meta-analyses that strict blood pressure control, particularly using ACE inhibitors or angiotensin II receptor blockers, together with rigorous control of diabetes, is effective in preventing progression to ESRD.[243] In a remote community in Northern Australia, a community-based cardiovascular and renal protective program was shown to be effective in reducing premature death and progression to ESRD among Indigenous adults with early renal disease.[255] The program was based on 1) the use of ACE inhibitors, combined with other antihypertensives, if needed, to achieve blood pressure goals; 2) attempts to improve control of blood glucose and lipid levels; and 3) health education. Screening programs in remote communities have consistently found that at least 25% of adults have macroalbuminuria.[149,161,205] Despite this indisputable evidence, there has been no coordinated national approach to providing secondary prevention services at a community level.

There is also clear evidence of reduced access to tertiary ESRD treatment services. Forty-eight per cent of Indigenous ESRD patients starting treatment during 1993-1998 lived in regions without ESRD treatment facilities.[24] Many needed to travel hundreds of kilometres to obtain renal care. By contrast, virtually all non-Indigenous patients (99.8%) lived in regions with ESRD treatment facilities. Indigenous ESRD patients are more likely to be referred to a nephrologist late in the course of their renal disease.[111] Late referral is associated with increased mortality on ESRD treatment[138] and is more common in disadvantaged areas.[256]

Indigenous Australian ESRD patients also suffer significantly reduced access to renal transplantation which is not explained by differences in age, sex, co-

morbidities or cause of renal disease.[257] This finding is consistent with US research focused on African Americans' access to transplantation, which suggests that disparities in access are not accounted for by differences in medical suitability or patient preferences.[115,117] It is also consistent with recent research indicating a disparity in the use of diagnostic and therapeutic procedures for Indigenous and non-Indigenous patients in Australian public hospitals. This suggests that there might be systematic differences in the treatment of Indigenous patients.[118] Further research is required to explore the contribution of this apparent racial discrimination to reduced access to ESRD treatment.

5. Linkage of cultural factors and renal disease

Cultural differences affect access to, and utilization of, health services. It has been suggested that a grossly deficient standard of cross-cultural communication has been accepted as the *norm* in some settings.[16] Patients' poor understanding of their own chronic renal disease has been linked to non-compliance and reduced active involvement in their own management.[16] In a recent qualitative study investigating the effectiveness of communication in ESRD care, a picture emerged of pervasive miscommunication, often unrecognised by both the patients and their health carers.[258] A shared understanding of fundamental issues concerning prevention, diagnosis and treatment was rarely achieved. Other research has suggested that the communication gap might be so wide, and so ingrained in health care, that it is not even perceived by staff.[94] Effective communication has been shown to correlate with improved outcomes, including physiological criteria such as adequacy of blood pressure and blood sugar control.[86] Therefore, grossly ineffective communication is likely to impede attempts to retard the progression of renal damage to ESRD.

6. Linkage of government and corporate policies to renal disease

Australian governments have attempted to address the social disadvantage of Indigenous Australians, but with limited success. Large-scale infrastructure

development has occurred in some communities, with projects designed to ensure adequate water supply, sanitation, housing and drainage.[43] However, a recent survey of houses funded by the Indigenous Housing Authority of the Northern Territory showed that 62% of houses did not meet the required standards for the storage and preparation of food, and that, in 45% of houses, bath and toilet facilities were not functional.[43] A recent review of education strategies revealed deteriorating outcomes, with an overall decline in school attendance and very low proportions of students achieving national reading benchmarks in primary school.[44] We have discussed above the linkage between both housing conditions and educational outcomes and the development of ESRD.

Corporate policies might also be playing an adverse role. As noted above, the prevalence of tobacco use is much higher among Indigenous Australians. There is evidence of tobacco advertising campaigns specifically targeting this group.[242] The promotion, in some Indigenous communities, of particular cigarette brands, with the distribution of 'giveaway' products, such as T-shirts, has been reported, and tobacco companies are prominent in the sponsorship of remote community sporting events. This is consistent with the aggressive marketing tactics used to target Indigenous populations of other South Pacific nations.[242] We have discussed above the various pathways linking tobacco use with the initiation and progression of renal disease.

We have outlined six discrete pathways linking disadvantage and kidney disease and others are likely to exist. It is clear that an ecosocial multi-level framework is both appropriate and useful in understanding ESRD among Indigenous Australians. How might this understanding inform an evidence-based approach to the prevention of ESRD?

9.9: A life-course approach to the prevention of ESRD

Nephrologists understand ESRD from a traditional, biomedical perspective, in which ESRD is attributed to one of a range of discrete primary disease processes. This view is inconsistent with the pathophysiological model which we have proposed. A limited biomedical perspective cannot explain the striking social gradient in the incidence of ESRD in Indigenous Australians. An integrated model such as that shown in Figure 9.1 enables us to bring together an understanding of the social, cultural and environmental determinants of health with an understanding of the biology of renal disease. A better understanding of the discrete pathways linking disadvantage and discrimination to their biological embodiment across the life-course,[224] enables us to identify targeted prevention programs to address this excess burden of renal disease.

Individual-level interventions alone, using pharmacological and lifestyle interventions for people at high-risk, are necessary but not sufficient to address the many determinants operating at the individual, community, regional and national levels. Primary preventive initiatives must address the period from before conception to the development of albuminuria. Such initiatives should include: improved access to antenatal services to reduce the prevalence of IUGR; community initiatives such as the Strong Women, Strong Babies, Strong Culture Program which resulted in improvement in birth weights in pilot communities;[259] early childhood development initiatives to improve educational achievement and life-skills; training community members to improve housing infrastructure and to maintain the improvements,[260] thus also providing employment opportunities; community-based scabies control programs; and legislative initiatives to regulate tobacco advertising.

Secondary prevention, covering the period from the development of albuminuria to ESRD, will require a coordinated, national program to provide community-based screening and intervention for high-risk groups. Strict control of blood pressure with ACE inhibitors as first-line therapy, and of

diabetes with oral hypoglycaemics and insulin, has been demonstrated to be effective in preventing progression to ESRD.[255] Accumulating evidence, albeit not among Indigenous Australians, suggests that smoking cessation and lipid lowering[261] might also be effective strategies. Improved, early access to nephrological services might prevent progression to ESRD, and should, with appropriate ESRD treatment, improve outcomes.[138]

While tertiary prevention initiatives, such as improved access to renal transplantation, are also required to improve ESRD treatment outcomes, an emphasis on primary and secondary prevention would result in improvements in health above and beyond the prevention or amelioration of ESRD.

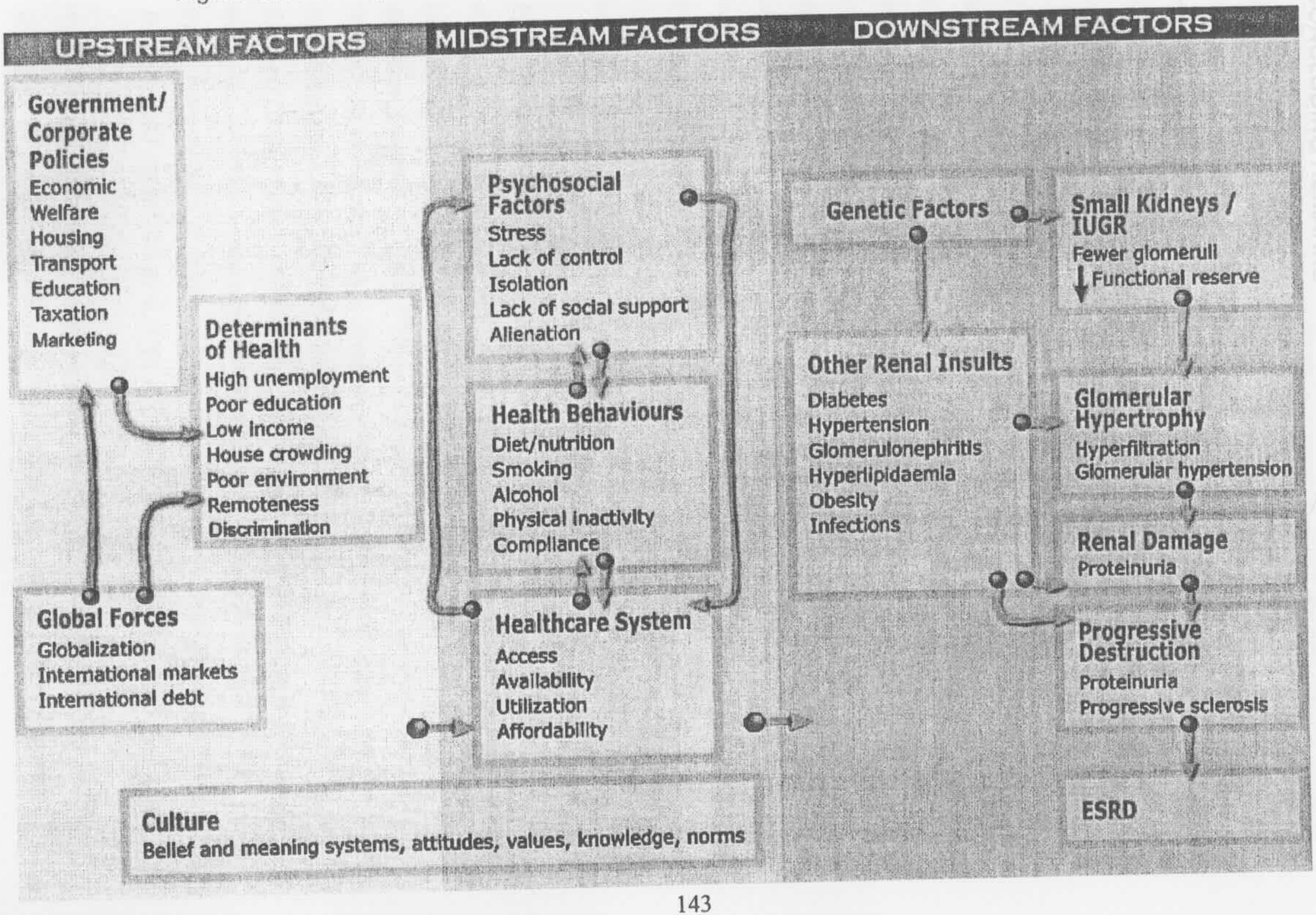
It is likely that the model we have developed is relevant to an understanding of patterns of renal disease in other high-risk populations. Furthermore, similar pathways might be relevant to other chronic diseases, such as diabetes and cardiovascular disease, among Indigenous Australians, as well as in other Indigenous populations in New Zealand, the United States and Canada and in developing countries. As we are able to confirm the many pathways from disadvantage to human biology, we are better placed to advocate evidence-based interventions, both within and beyond the scope of the healthcare system, to address the excess burden of renal disease in Indigenous Australians and other affected groups. This would provide a more fundamental solution than simply building a dialysis unit and a better long-term answer the call for help made by the people of Kintore and Kiwirrkura.

Table 9.1: **Attributed primary cause of ESRD for new Australian ESRD patients, 1993-98***

Cause	Indigenous (n=719)	Non-Indigenous (n=7,409)	P value
Diabetes	322 (44.8%)	1,281 (17.3%)	<0.001
Glomerulonephritis	204 (28.4%)	2,535 (34.2%)	0.001
Uncertain	100 (13.9%)	436 (5.9%)	<0.001
Hypertension	35 (4.9%)	837 (11.3%)	<0.001
Miscellaneous	31 (4.3%)	813 (11.0%)	<0.001
Reflux	13 (1.8%)	396 (5.3%)	<0.001
Analgesic use	8 (1.1%)	552 (7.5%)	<0.001
Polycystic kidney disease	6 (0.8%)	559 (7.5%)	<0.001

*Data sourced from ANZDATA Registry, 2001

Figure 9.1: An integrated model of end-stage renal disease in Indigenous Australians



CONCLUDING REMARKS

In this thesis, I have explored the social determinants of end-stage renal disease and focused on these as an explanation of the excess burden of renal disease among Indigenous Australians. It is generally assumed that their high incidence of renal disease is due to a high incidence of diabetes and a yet to be defined genetic predisposition. During the four years of my research in the Northern Territory, I came to realise that patterns of disease in indigenous populations are fundamentally shaped by socioeconomic and cultural forces.

This understanding is inconsistent with modern nephrological concepts of disease causation. I have demonstrated the strong relationship, among Indigenous Australians, between disadvantage and ESRD incidence and also between disadvantage and lack of access to effective prevention and treatment services. As a nephrologist, my aim has been to explain how disadvantage is biologically incorporated into the pathophysiological processes which culminate in end-stage renal disease. In this way, the insights provided by sociology on the one hand, and by medical science on the other, may be brought together to reach a more fundamental understanding of the causes of the 'epidemic of renal disease' amongst Indigenous Australians.

The model developed in this thesis is likely to be relevant to an understanding of patterns of renal disease in other high-risk populations. Furthermore, similar pathways might be relevant, among Indigenous populations throughout the developed world and among the populations of developing countries, to other chronic diseases, such as diabetes and cardiovascular disease. If we are able to confirm the many pathways from disadvantage to human biology through this and other related research, we might be better placed to advocate evidence-based interventions, both within and beyond the scope of the healthcare system, to address the excess burden of renal disease in Indigenous Australians and other affected groups.

These research findings have implications for the provision of health services designed to prevent chronic disease, for the equitable delivery of quality

ESRD treatment services to Indigenous Australians, and for adopting a 'whole of government' approach to reduce the excess burden of chronic diseases in disadvantaged, high-risk populations.

As a result of undertaking this research, I have become involved in a series of national initiatives in the delivery of renal services.

I have been instrumental in bringing together a multi-disciplinary team in Darwin, Brisbane and Sydney to undertake research leading to improvements in equity and quality of health care delivery to Indigenous Australians with renal disease. We have developed a multi-centre research study, the IMPAKT (Improving Indigenous Patients' Access to Kidney Transplantation) study, to explore the reasons for the disparities in access to transplantation which have been demonstrated in this research. This project has been submitted to the National Health and Medical Research Council and Australian Kidney Foundation for funding. As a 2002-2003 Harkness Fellow in Health Policy, I will undertake a cross-national study of ethnic minorities' access to renal transplantation at the Department of Health Care Policy in the Harvard Medical School.

I have been consulted by, and addressed, the Office of Aboriginal and Torres Strait Islander Health, the Northern Territory Department of Health and Community Services, the New South Wales Department of Health, and the ATSIC regional executives in Darwin and East Arnhem regarding the delivery of ESRD treatment services and prevention services for Indigenous Australians.

The research examining the effects of late referral on dialysis outcomes led to my approaching Dr John Knight, at that time the Medical Director of the Australian Kidney Foundation, to propose that we address the quality of pre-ESRD care in Australia. He and I submitted a discussion paper to the Australian Kidney Foundation and to the Australia and New Zealand Society of Nephrology proposing the establishment of a taskforce to address

awareness, and management, of chronic renal insufficiency in general practice. The Kidney Check Australia Taskforce first met in March 2001. Two papers in the Appendices indicate some of the output from the Taskforce.

REFERENCES

1. Glover J, Harris K, Tennant S. A Social Health Atlas of Australia. Second ed. Adelaide: Public Health Information Development Unit, University of Adelaide, 1999.

2. Sexton PT, Sexton TL. Excess coronary mortality among Australian men and women living outside the capital city statistical divisions. *Med J Aust* 2000;**172**(8):370-4.

3. National Health Strategy. Enough to make you sick: how income and environment affect health, Research Paper No. 1. Melbourne: National Health Strategy Unit, 1992.

4. Taylor R, Chey T, Bauman A, Webster I. Socio-economic, migrant and geographic differentials in coronary heart disease occurrence in New South Wales. *Aust N Z J Public Health* 1999;**23**(1):20-6.

5. Turrell G, Mathers CD. Socioeconomic status and health in Australia. *Med J Aust* 2000;**172**(9):434-8.

6. Heller RF. Mortality from cardiovascular disease is too high outside capital cities [editorial]. *Med J Aust* 2000;**172**(8):360-1.

7. McLaren B. Renal failure in Arnhem Land: missed opportunities for prevention and treatment. *Aust J Rural Health* 1996;**4**(2):61-6.

8. Lowe M, Kerridge IH, Mitchell KR. 'These sorts of people don't do very well': race and allocation of health care resources. *J Med Ethics* 1995;**21**(6):356-60.

9. Disney A, Russ G, Walker R, Collins J, Herbert K, Kerr P, eds. ANZDATA Registry Report 1999. Adelaide: Australia and New Zealand Dialysis and Transplant Registry, 2000.

10. Cass A, McDonald SP, Wang Z. Australians with renal disease: a new national survey. *Med J Aust* 1999;**171**(8):444.

11. Spencer JL, Silva DT, Snelling P, Hoy WE. An epidemic of renal failure among Australian Aboriginals. *Med J Aust* 1998;**168**(11):537-41.

12. Australian Bureau of Statistics. Population issues, Indigenous Australians. Canberra: Australian Bureau of Statistics, 1999.

13. Australian Bureau of Statistics. Experimental estimates of the Aboriginal and Torres Strait Islander population. Canberra: Australian Bureau of Statistics, 1998.
14. Schmidt B. Northern Zone Renal Services Plan 2000-2010, 2000.
15. Devitt J, McMasters A. On the machine: Aboriginal stories about kidney troubles. Alice Springs: IAD Press, 1998.
16. Devitt J, McMasters A. Living on medicine: a cultural study of end-stage renal disease among Aboriginal people. Alice Springs: IAD Press, 1998.
17. Krieger N, Williams DR, Moss NE. Measuring social class in US public health research: concepts, methodologies, and guidelines. *Annu Rev Public Health* 1997;**18**:341-78.
18. Marmot M. Social determinants of health: from observation to policy. *Med J Aust* 2000;**172**(8):379-82.
19. Turrell G, Oldenburg B, McGuffog I, Dent R. Socioeconomic determinants of health: towards a national research program and a policy and intervention agenda. Canberra: Queensland University of Technology, School of Public Health, Ausinfo, 1999.
20. Parmer RJ, Stone RA, Cervenka JH. Renal hemodynamics in essential hypertension. Racial differences in response to changes in dietary sodium. *Hypertension* 1994;**24**(6):752-7.
21. Hoy WE, Rees M, Kile E, Mathews JD, Wang Z. A new dimension to the Barker hypothesis: low birthweight and susceptibility to renal disease. *Kidney Int* 1999;**56**(3):1072-7.
22. Lopes AA, Port FK. The low birth weight hypothesis as a plausible explanation for the black/white differences in hypertension, non-insulin-dependent diabetes, and end-stage renal disease. *Am J Kidney Dis* 1995;**25**(2):350-6.
23. Australian Bureau of Statistics and Australian Institute of Health and Welfare. The health and welfare of Australia's Aboriginal and Torres Strait Islander peoples. Canberra: Australian Bureau of Statistics, 1999.
24. Cass A, Cunningham J, Wang Z, Hoy W. Regional variation in the incidence of end-stage renal disease in Indigenous Australians. *MJA* 2001;**175**(1):24-27.

25. Disney A, ed. ANZDATA Registry Report 2000. Adelaide: Australia and New Zealand Dialysis and Transplant Registry, 2001.
26. Maisonneuve P, Agodoa L, Gellert R, et al. Distribution of primary renal diseases leading to end-stage renal failure in the United States, Europe, and Australia/New Zealand: results from an international comparative study. *Am J Kidney Dis* 2000;**35**(1):157-65.
27. Vinson T. Unequal in life: the distribution of social disadvantage in Victoria and New South Wales. Melbourne: The Ignatius Centre for social policy and research, 1999.
28. Australian Bureau of Statistics. Socio-economic indexes for areas. Canberra: Australian Bureau of Statistics, 1998.
29. Morris R, Carstairs V. Which deprivation? A comparison of selected deprivation indexes. *J Public Health Med* 1991;**13**(4):318-26.
30. Australian Bureau of Statistics. Australian Bureau of Statistics special tabulation request: Australian Bureau of Statistics, 2000.
31. Australian Bureau of Statistics. Census of population and housing: Aboriginal and Torres Strait Islander people. Canberra: Australian Bureau of Statistics, 1998.
32. Day P, Sullivan EA, Lancaster P. Indigenous mothers and their babies Australia 1994-1996. Sydney: Australian Institute of Health and Welfare National Perinatal Statistics Unit, 1999.
33. Australian Bureau of Statistics. Labour force characteristics of Aboriginal and Torres Strait Islander Australians. Canberra: Australian Bureau of Statistics, 2000.
34. Mackenbach JP, Kunst AE. Measuring the magnitude of socio-economic inequalities in health: an overview of available measures illustrated with two examples from Europe. *Soc Sci Med* 1997;**44**(6):757-71.
35. Turrell G, Mathers CD. Socioeconomic inequalities in all-cause and specific-cause mortality in Australia: 1985-1987 and 1995-1997. *International Journal of Epidemiology* 2001;**30**:231-239.
36. Cass A, Cunningham J, Wang Z, Hoy W. Social disadvantage and variation in the incidence of end-stage renal disease in Australian capital cities. *Aust N Z J Public Health* 2001;**25**(4):322-6.

37. Khan IH, Cheng J, Catto GR, Edward N, MacLeod AM. Social deprivation indices of patients on renal replacement therapy (RRT) in Grampian. *Scott Med J* 1993;**38**(5):139-41.
38. Byrne C, Nedelman J, Luke RG. Race, socioeconomic status, and the development of end-stage renal disease. *Am J Kidney Dis* 1994;**23**(1):16-22.
39. Young EW, Mauger EA, Jiang KH, Port FK, Wolfe RA. Socioeconomic status and end-stage renal disease in the United States. *Kidney Int* 1994;**45**(3):907-11.
40. Perneger TV, Whelton PK, Klag MJ. Race and end-stage renal disease. Socioeconomic status and access to health care as mediating factors. *Arch Intern Med* 1995;**155**(11):1201-8.
41. Australian Kidney Foundation & Australia New Zealand Society of Nephrology. The CARI Guidelines (Caring for Australians with Renal Impairment). 2001.
42. Kuh D, Ben-Shlomo Y. A life course approach to chronic disease epidemiology. Oxford ; New York: Oxford University Press, 1997.
43. Bailie R, Runcie M. Household infrastructure in Aboriginal communities and the implications for health improvement. *Med J Aust* 2001;**175**(7):363-366.
44. Collins B. Learning lessons: an independent review of Indigenous education in the Northern Territory. Darwin: Northern Territory Department of Education, 1999.
45. Altman J, Gray M. The effects of the CDEP scheme on the economic status of Indigenous Australians: some analyses using the 1996 Census. Canberra: Centre for Aboriginal Economic Policy Research, The Australian National University., 2000.
46. Spicer I. Independent Review of the Community Development Employment Projects (CDEP) Scheme. Canberra: Aboriginal and Torres Strait Islander Commission, 1997.
47. Aboriginal and Torres Strait Islander Commission. Aboriginal and Torres Strait Islander Commission Annual Report 1999-2000. Canberra: Aboriginal and Torres Strait Islander Commission, 2000.

48. The Office of the Aboriginal and Torres Strait Islander Social Justice Commissioner. Social justice report 2000. Sydney: Human Rights and Equal Opportunity Commission, 2001.
49. Australian Institute of Health and Welfare. Health in rural and remote Australia. Canberra: AIHW, 1998.
50. Australian Bureau of Statistics. Australian Standard Geographical Classification. Canberra: Australian Bureau of Statistics, 1999.
51. Australian Bureau of Statistics. 1996 Census of Population and Housing: Socio-economic Indexes for Areas. Canberra: Australian Bureau of Statistics, 1998.
52. Schena FP. Epidemiology of end-stage renal disease: International comparisons of renal replacement therapy. *Kidney International* 2000;**57**(Suppl. 74):S39-45.
53. Baigent C, Burbury K, Wheeler D. Premature cardiovascular disease in chronic renal failure. *Lancet* 2000;**356**(9224):147-52.
54. Prichard SS. Comorbidities and their impact on outcome in patients with end-stage renal disease. *Kidney International* 2000;**57**(Suppl. 74):S100-S104.
55. Sesso R, Belasco AG. Late diagnosis of chronic renal failure and mortality on maintenance dialysis. *Nephrol Dial Transplant* 1996;11(12):2417-20.
56. Arora P, Obrador GT, Ruthazer R, et al. Prevalence, predictors, and consequences of late nephrology referral at a tertiary care center. *J Am Soc Nephrol* 1999;**10**(6):1281-6.
57. Jungers P, Zingraff J, Albouze G, et al. Late referral to maintenance dialysis: detrimental consequences. *Nephrol Dial Transplant* 1993;**8**(10):1089-93.
58. Roubicek C, Brunet P, Huiart L, et al. Timing of nephrology referral: influence on mortality and morbidity [see comments]. *Am J Kidney Dis* 2000;**36**(1):35-41.
59. Schmidt RJ, Domico JR, Sorkin MI, Hobbs G. Early referral and its impact on emergent first dialyses, health care costs, and outcome. *Am J Kidney Dis* 1998;32(2):278-83.
60. Khan IH, Catto GR, Edward N, MacLeod AM. Chronic renal failure: factors influencing nephrology referral. *QJM* 1994;**87**(9):559-64.

61. Ifudu O, Dawood M, Iofel Y, Valcourt JS, Friedman EA. Delayed referral of black, Hispanic, and older patients with chronic renal failure. *Am J Kidney Dis* 1999;**33**(4):728-33.
62. Chandna SM, Schulz J, Lawrence C, Greenwood RN, Farrington K. Is there a rationale for rationing chronic dialysis? A hospital based cohort study of factors affecting survival and morbidity. *BMJ* 1999;**318**(7178):217-23.
63. Levin A. Consequences of late referral on patient outcomes. *Nephrol Dial Transplant* 2000;**15**(Suppl 3(6)):8-13.
64. Shemin D, Bostom A, Laliberty P, Dworkin L. Residual renal function and mortality risk in hemodialysis patients. *Am J Kidney Dis* 2001;**38**(1):85-90.
65. Ruggenenti P, Perna A, Gherardi G, et al. Renoprotective properties of ACE-inhibition in non-diabetic nephropathies with non-nephrotic proteinuria. *Lancet* 1999;**354**(9176):359-64.
66. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. The Collaborative Study Group. *N Engl J Med* 1993;**329**(20):1456-62.
67. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med* 2001;**345**(12):861-9.
68. Klahr S, Levey AS, Beck GJ, et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group. *N Engl J Med* 1994;**330**(13):877-84.
69. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;**329**(14):977-86.
70. Eadington DW. Delayed referral for dialysis [editorial]. *Nephrol Dial Transplant* 1996;11(11):2124-6.
71. Campbell JD, Ewigman B, Hosokawa M, Van Stone JC. The timing of referral of patients with end-stage renal disease. *Dial Transplant* 1989;**18**:660-686.

72. Knight J, Vimalachandra D, eds. The CARI guidelines - caring for Australians with renal impairment. Sydney: Excerpta Medica Communications, 2000.
73. Australian Diabetes Obesity and Lifestyle Study, Dunstan DW, International Diabetes Institute. Diabesity & associated disorders in Australia - 2000: the accelerating epidemic. Melbourne: International Diabetes Institute, 2001.
74. Iseki K, Iseki C, Ikemiya Y, Fukiyama K. Risk of developing end-stage renal disease in a cohort of mass screening. *Kidney Int* 1996;**49**(3):800-5.
75. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976;**16**(1):31-41.
76. Challah S, Wing AJ, Bauer R, Morris RW, Schroeder SA. Negative selection of patients for dialysis and transplantation in the United Kingdom. *BMJ* 1984;**288**(6424):1119-22.
77. Fraser S, Bunce C, Wormald R, Brunner E. Deprivation and late presentation of glaucoma: case-control study. *Bmj* 2001;**322**(7287):639-43.
78. NIH Consensus Development Conference Panel. Morbidity and mortality of renal dialysis: an NIH consensus conference statement. *Ann Intern Med* 1994;**121**(1):62-70.
79. Van Biesen W, Wiedemann M, Lameire N. End-stage renal disease treatment: a European perspective. *J Am Soc Nephrol* 1998;**9**:S55-S62.
80. Lameire N, Van Biesen W. The pattern of referral of patients with end-stage renal disease to the nephrologist--a European survey. *Nephrol Dial Transplant* 1999;**14**(Suppl 6):16-23.
81. Centre for Disease Control and Prevention. End-stage renal disease attributed to diabetes among American Indians/ Alaskan Natives with diabetes --- United States, 1990 -- 1996. *Morbidity Mortality weekly Report* 2000;**49**(42):959-962.
82. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Stamler J. End-stage renal disease in African-American and white men. 16-year MRFIT findings. *Jama* 1997;**277**(16):1293-8.
83. Tell GS, Hylander B, Craven TE, Burkart J. Racial differences in the incidence of end-stage renal disease. *Ethn Health* 1996;1(1):21-31.

84. Royal Australian College of General Practitioners. Guidelines for prevention activities in general practice. 5th edition. Melbourne: Royal Australian College of General Practitioners, 2001.
85. Ong LM, de Haes JC, Hoos AM, Lammes FB. Doctor-patient communication: a review of the literature. *Soc Sci Med* 1995;**40**(7):903-18.
86. Stewart MA. Effective physician-patient communication and health outcomes: a review. *Cmaj* 1995;**152**(9):1423-33.
87. Putsch RW. Cross-cultural communication. The special case of interpreters in health care. *Jama* 1985;**254**(23):3344-8.
88. Dollis N, National Health Strategy (Australia). Removing cultural and language barriers to health. [Melbourne]: National Health Strategy, 1993.
89. Lowell A. Communication and cultural knowledge in Aboriginal health care. Darwin: Cooperative Research Centre for Aboriginal and Tropical Health., 2001.
90. Australian Royal Commission into Aboriginal Deaths in Custody, Johnston E. National report : overview and recommendations. Canberra: Australian Govt. Pub. Service, 1991.
91. Humphery K, Weeramanthri T, Fitz J. Forgetting compliance: Aboriginal health and medical culture. Darwin: Northern Territory University Press in conjunction with the Cooperative Research Centre for Aboriginal and Tropical Health, 2001.
92. Mobbs R. But I do care! Communication difficulties affecting the quality of care delivered to aborigines. *Med J Aust* 1986;**144 Suppl**:S3-5.
93. Edis F. 'Just scratching the surface': miscommunication in Aboriginal health care. Master of Education: Northern Territory University, 1998.
94. Trudgen R. Why warriors lie down and die. Darwin: Aboriginal Resource and Development Services Inc., 2000.
95. Cooke M. Anglo/Yolgnu communication in the criminal justice system. PhD thesis: University of New England, 1998.
96. Pope C, Ziebland S, Mays N. Qualitative research in health care. Analysing qualitative data. *Bmj* 2000;**320**(7227):114-6.
97. Meyer J. Qualitative research in health care. Using qualitative methods in health related action research. *Bmj* 2000;**320**(7228):178-81.

98. Higginbotham N, Albrecht G, Connor L. Health Social Science: a transdisciplinary and complexity perspective. Melbourne: Oxford University Press, 2001.
99. Mays N, Pope C. Qualitative research in health care. Assessing quality in qualitative research. *Bmj* 2000;**320**(7226):50-2.
100. Barbour RS. Checklists for improving rigour in qualitative research: a case of the tail wagging the dog? *Bmj* 2001;**322**(7294):1115-7.
101. Eades D. Communicative Strategies in Aboriginal English. In: Romaine S, ed. Language in Australia. Cambridge ; New York: Cambridge University Press, 1991.
102. Campbell DA. Hope and harm: a delicate balance. *MJA* 2001;**175**(10):540-541.
103. Steffensen MS, Colker L. Intercultural misunderstandings about health care. Recall of descriptions of illness and treatment. *Soc Sci Med* 1982;**16**(22):1949-54.
104. ANZDATA Registry. Special data request, 2001.
105. Eggers PW. Effect of transplantation on the Medicare end-stage renal disease program. *N Engl J Med* 1988;**318**(4):223-9.
106. Evans RW, Manninen DL, Garrison LP, Jr., et al. The quality of life of patients with end-stage renal disease. *N Engl J Med* 1985;**312**(9):553-9.
107. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 1999;**341**(23):1725-30.
108. U.S. Renal Data System. 2001 Annual Data Report: Atlas of End-Stage Renal Disease in the United States. Bethesda: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2001.
109. Alexander GC, Sehgal AR. Barriers to cadaveric renal transplantation among blacks, women, and the poor. *Jama* 1998;**280**(13):1148-52.
110. Alexander GC, Sehgal AR. Why haemodialysis patients fail to complete the transplantation process. *Am J Kidney Dis* 2001;**37**(2):321-328.
111. Cass A, Snelling P, Cunningham J, Wang Z, Hoy W. Timing of nephrology referral: A study of its effect on the likelihood of transplantation and impact on mortality. *Nephrology* 2002;**7**:S29-S32.

112. Briganti EM, Wolfe R, Russ GR, Eris JM, Walker RG, McNeil JJ. Centre effect in renal transplantation in Australia 1993 - 1998. In: Russ GR, ed. ANZDATA Registry Report 2001. Adelaide: Australia and New Zealand Dialysis and Transplant Registry, 2002.
113. McDonald SP, Russ GR. The burden of end-stage renal disease among Indigenous peoples in Australia and New Zealand. In: Russ GR, ed. ANZDATA Registry Report 2001. Adelaide: Australia and New Zealand Dialysis and Transplant Registry, 2002: 96-99.
114. Chertow G, Zenios S. Gridlock on the road to kidney transplantation. *Am J Kidney Dis* 2001;**37**(2):435-7.
115. Ayanian JZ, Cleary PD, Weissman JS, Epstein AM. The effect of patients' preferences on racial differences in access to renal transplantation. *N Engl J Med* 1999;**341**(22):1661-9.
116. Thamer M, Hwang W, Fink NE, et al. U.S. nephrologists' attitudes towards renal transplantation: results from a national survey. *Transplantation* 2001;**71**(2):281-8.
117. Epstein AM, Ayanian JZ, Keogh JH, et al. Racial disparities in access to renal transplantation--clinically appropriate or due to underuse or overuse? *N Engl J Med* 2000;**343**(21):1537-44.
118. Cunningham J. Diagnostic and therapeutic procedures among Australian hospital patients identified as Indigenous. *MJA* 2002;**176**(2):58-62.
119. Leppert PC, Partner SF, Thompson A. Learning from the community about barriers to health care. *Obstet Gynecol* 1996;**87**(1):140-1.
120. Sless D. Usable written information for patients. *Med J Aust* 2001;**174**(11):557-8.
121. Stephenson PH. Vietnamese refugees in Victoria, B.C.: an overview of immigrant and refugee health care in a medium-sized Canadian urban centre. *Soc Sci Med* 1995;**40**(12):1631-42.
122. Arai Y, Farrow S. Access, expectations and communication: Japanese mothers' interaction with GPs in a pilot study in North London. *Public Health* 1995;**109**(5):353-61.

123. National Work Group on Literacy and Health. Communicating with patients who have limited literacy skills. Report of the National Work Group on Literacy and Health. *J Fam Pract* 1998;46(2):168-76.
124. Young CJ, Gaston RS. Renal transplantation in black Americans. *N Engl J Med* 2000;343(21):1545-52.
125. Transplantation Society of Australia and New Zealand. General organ donor criteria: kidney allocation and distribution. At http://www.racp.edu/tsanz/oap, 2000.
126. National Organ Matching Service. National organ matching system: algorithms used in kidney matching, 2001.
127. Anderson I. The ethics of the allocation of health resources. In: Cowlishaw G, Morris B, eds. Race matters Indigenous Australians and 'our' society: Aboriginal Studies Press, 1997: 191-208.
128. Takemoto SK, Terasaki PI, Gjertson DW, Cecka JM. Twelve years' experience with national sharing of HLA-matched cadaveric kidneys for transplantation. *N Engl J Med* 2000;343(15):1078-84.
129. Held PJ, Kahan BD, Hunsicker LG, et al. The impact of HLA mismatches on the survival of first cadaveric kidney transplants. *N Engl J Med* 1994;331(12):765-70.
130. Delmonico FL, Milford EL, Goguen J, et al. A novel united network for organ sharing region kidney allocation plan improves transplant access for minority candidates. *Transplantation* 1999;68(12):1875-9.
131. Russ GR, ed. ANZDATA Registry Report 2001. Adelaide: Australia and New Zealand Dialysis and Transplant Registry, 2002.
132. Australian Institute of Health and Welfare. Australia's health 2002. Canberra: Australian Institute of Health and Welfare, 2002.
133. Cunningham J, Paradies Y. Occasional paper: Mortality of Aboriginal and Torres Strait Islander Australians. ABS cat. no. 3315.0. Canberra: Australian Bureau of Statistics, 2000.
134. Dyck RF. Mechanisms of renal disease in indigenous populations: influences at work in Canadian indigenous peoples. *Nephrology* 2001;6(1):3-7.

135. Cass A, Cunningham J, Snelling P, Wang Z, Hoy W. End-stage renal disease in Indigenous Australians: a disease of disadvantage. *Ethnicity and Disease* 2002;12(3):373-378.
136. Perneger TV, Brancati FL, Whelton PK, Klag MJ. Studying the causes of kidney disease in humans: a review of methodological obstacles and possible solutions. *Am J Kidney Dis* 1995;25(5):722-31.
137. Perneger TV, Whelton PK, Klag MJ, Rossiter KA. Diagnosis of hypertensive end-stage renal disease: effect of patient's race. *Am J Epidemiol* 1995;141(1):10-5.
138. Cass A, Cunningham J, Arnold P, Snelling P, Wang Z, Hoy W. Delayed referral to a nephrologist: outcomes among those who survive at least one year on dialysis. *MJA* 2002;177(3):135-138.
139. Stiles KP, Yuan CM, Chung EM, Lyon RD, Lane JD, Abbott KC. Renal biopsy in high-risk patients with medical diseases of the kidney. *Am J Kidney Dis* 2000;36(2):419-33.
140. Iyengar SK, Schelling JR, Sedor JR. Approaches to understanding susceptibility to nephropathy: From genetics to genomics. *Kidney Int* 2002;61 Suppl 1:61-7.
141. Freedman BI. End-stage renal failure in African Americans: insights in kidney disease susceptibility. *Nephrol Dial Transplant* 2002;17(2):198-200.
142. Fogarty DG, Rich SS, Hanna L, Warram JH, Krolewski AS. Urinary albumin excretion in families with type 2 diabetes is heritable and genetically correlated to blood pressure. *Kidney Int* 2000;57(1):250-7.
143. Freedman BI, Bowden DW, Rich SS, Appel RG. Genetic initiation of hypertensive and diabetic nephropathy. *Am J Hypertens* 1998;11(2):251-7.
144. Schelling JR, Zarif L, Sehgal A, Iyengar S, Sedor JR. Genetic susceptibility to end-stage renal disease. *Curr Opin Nephrol Hypertens* 1999;8(4):465-72.
145. Lei HH, Perneger TV, Klag MJ, Whelton PK, Coresh J. Familial aggregation of renal disease in a population-based case-control study. *J Am Soc Nephrol* 1998;9(7):1270-6.

146. Pettitt DJ, Saad MF, Bennett PH, Nelson RG, Knowler WC. Familial predisposition to renal disease in two generations of Pima Indians with type 2 (non-insulin-dependent) diabetes mellitus. *Diabetologia* 1990;**33**(7):438-43.
147. Hoy WE, Megill DM, Hughson MD. Epidemic renal disease of unknown etiology in the Zuni Indians. *Am J Kidney Dis* 1987;**9**(6):485-96.
148. Van Buynder PG, Gaggin JA, Mathews JD. Renal disease patterns in aboriginal Australians. A family-based study in a high incidence community. *Med J Aust* 1993;**159**(2):82-7.
149. Hoy WE, Mathews JD, McCredie DA, et al. The multidimensional nature of renal disease: rates and associations of albuminuria in an Australian Aboriginal community. *Kidney Int* 1998;**54**(4):1296-304.
150. Nelson RG. Diabetic renal disease in transitional and disadvantaged populations. *Nephrology* 2001;**6**(1):9-17.
151. Neel JV. Diabetes mellitus: a "thrifty" genotype rendered detrimental by "progress"? *Am J Human Genetics* 1962;**14**:353-362.
152. Williams DR, Moffitt PS, Fisher JS, Bashir HV. Diabetes and glucose tolerance in New South Wales coastal Aborigines: possible effects of non-Aboriginal genetic admixture. *Diabetologia* 1987;**30**(2):72-7.
153. Neel JV. The "thrifty genotype" in 1998. *Nutr Rev* 1999;**57**(5 Pt 2):S2-9.
154. Dudley CR, Keavney B, Stratton IM, Turner RC, Ratcliffe PJ. U.K. Prospective Diabetes Study. XV: Relationship of renin-angiotensin system gene polymorphisms with microalbuminuria in NIDDM. *Kidney Int* 1995;**48**(6):1907-11.
155. Parving HH, Jacobsen P, Tarnow L, et al. Effect of deletion polymorphism of angiotensin converting enzyme gene on progression of diabetic nephropathy during inhibition of angiotensin converting enzyme: observational follow up study. *Bmj* 1996;**313**(7057):591-4.
156. Yoshida H, Kuriyama S, Atsumi Y, et al. Angiotensin I converting enzyme gene polymorphism in non-insulin dependent diabetes mellitus. *Kidney Int* 1996;**50**(2):657-64.
157. Harden PN, Geddes C, Rowe PA, et al. Polymorphisms in angiotensin-converting-enzyme gene and progression of IgA nephropathy. *Lancet* 1995;**345**(8964):1540-2.

158. Schena FP, D'Altri C, Cerullo G, Manno C, Gesualdo L. ACE gene polymorphism and IgA nephropathy: an ethnically homogeneous study and a meta-analysis. *Kidney Int* 2001;60(2):732-40.
159. Schmidt S, Schone N, Ritz E. Association of ACE gene polymorphism and diabetic nephropathy? The Diabetic Nephropathy Study Group. *Kidney Int* 1995;47(4):1176-81.
160. Lester S, Heatley S, Bardy P, et al. The DD genotype of the angiotensin-converting enzyme gene occurs in very low frequency in Australian Aboriginals. *Nephrol Dial Transplant* 1999;14(4):887-90.
161. McDonald SP, Hoy WE, Maguire GP, Duarte NL, Wilcken DE, Wang XL. The p53Pro72Arg polymorphism is associated with albuminuria among aboriginal Australians. *J Am Soc Nephrol* 2002;13(3):677-83.
162. Imperatore G, Hanson RL, Pettitt DJ, Kobes S, Bennett PH, Knowler WC. Sib-pair linkage analysis for susceptibility genes for microvascular complications among Pima Indians with type 2 diabetes. Pima Diabetes Genes Group. *Diabetes* 1998;47(5):821-30.
163. Busfield F, Duffy DL, Kesting JB, et al. A genome wide search for type 2 diabetes-susceptibility genes in indigenous Australians. *Am J Hum Genet* 2002;70(2):349-57.
164. Baird PA. Genetic technologies and achieving health for populations. *Int J Health Serv* 2000;30(2):407-24.
165. Baird PA. The role of genetics in population health. In: Evans R.G, Barer M.L, Marmor T.R, eds. Why are some people healthy and others not? The determinants of health of populations. New York: Aldine de Gruyther, 1994: 133-159.
166. Williams DR. Race and health: basic questions, emerging directions [see comments]. *Ann Epidemiol* 1997;7(5):322-33.
167. American Association of Physical Anthropology. AAPA statement on biological aspects of race. *Am J Phys Anthropol* 1996;101:569-570.
168. Barker DJ, Osmond C. Infant mortality, childhood nutrition, and ischaemic heart disease in England and Wales. *Lancet* 1986;1(8489):1077-81.

169. Barker DJ, Osmond C. Death rates from stroke in England and Wales predicted from past maternal mortality. *Br Med J (Clin Res Ed)* 1987;**295**(6590):83-6.
170. Barker DJ, Osmond C. Inequalities in health in Britain: specific explanations in three Lancashire towns. *Br Med J (Clin Res Ed)* 1987;**294**(6574):749-52.
171. Barker DJ, Hales CN, Fall CH, Osmond C, Phipps K, Clark PM. Type 2 (non-insulin-dependent) diabetes mellitus, hypertension and hyperlipidaemia (syndrome X): relation to reduced fetal growth. *Diabetologia* 1993;**36**(1):62-7.
172. Barker DJ, Martyn CN. The maternal and fetal origins of cardiovascular disease. *J Epidemiol Community Health* 1992;**46**(1):8-11.
173. Hales CN, Barker DJ. Type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. *Diabetologia* 1992;**35**(7):595-601.
174. Brenner BM, Chertow GM. Congenital oligonephropathy and the etiology of adult hypertension and progressive renal injury. *Am J Kidney Dis* 1994;**23**(2):171-5.
175. Merlet-Benichou C, Vilar J, Lelievre-Pegorier M, Moreau E, Gilbert T. Fetal nephron mass: its control and deficit. *Adv Nephrol Necker Hosp* 1997;**26**:19-45.
176. Hinchliffe SA, Sargent PH, Howard CV, Chan YF, van Velzen D. Human intrauterine renal growth expressed in absolute number of glomeruli assessed by the disector method and Cavalieri principle. *Lab Invest* 1991;**64**(6):777-84.
177. Hinchliffe SA, Lynch MR, Sargent PH, Howard CV, Van Velzen D. The effect of intrauterine growth retardation on the development of renal nephrons. *Br J Obstet Gynaecol* 1992;**99**(4):296-301.
178. Bertram JF. Counting in the kidney. *Kidney Int* 2001;**59**(2):792-6.
179. Nyengaard JR, Bendtsen TF. Glomerular number and size in relation to age, kidney weight, and body surface in normal man. *Anat Rec* 1992;**232**(2):194-201.
180. Moore RA. The total number of glomeruli in the normal human kidney. *The Anatomical Record* 1931;**48**(1):153-168.
181. Tauchi H, Tsuboi K, Okutomi J. Age changes in the human kidney of the different races. *Gerontologia* 1971;**17**(2):87-97.

182. Brenner BM, Lawler EV, Mackenzie HS. The hyperfiltration theory: a paradigm shift in nephrology. *Kidney Int* 1996;**49**(6):1774-7.
183. Fogo AB. Glomerular hypertension, abnormal glomerular growth, and progression of renal diseases. *Kidney Int Suppl* 2000;**75**:S15-21.
184. Brenner BM, Garcia DL, Anderson S. Glomeruli and blood pressure. Less of one, more the other? *Am J Hypertens* 1988;**1**(4 Pt 1):335-47.
185. Lipschutz JH. Molecular development of the kidney: a review of the results of gene disruption studies. *Am J Kidney Dis* 1998;**31**(3):383-97.
186. Rauchman M. The role of homeobox genes in kidney development. *Curr Opin Nephrol Hypertens* 2000;**9**(1):37-42.
187. Resnik R. Intrauterine growth restriction. *Obstet Gynecol* 2002;**99**(3):490-6.
188. Sayers S, Powers J. Risk factors for aboriginal low birthweight, intrauterine growth retardation and preterm birth in the Darwin Health Region. *Aust N Z J Public Health* 1997;**21**(5):524-30.
189. Sayers SM, Powers JR. Birth size of Australian aboriginal babies. *Med J Aust* 1993;**159**(9):586-91.
190. Lelievre-Pegorier M, Merlet-Benichou C. The number of nephrons in the mammalian kidney: environmental influences play a determining role. *Exp Nephrol* 2000;**8**(2):63-5.
191. Zeman FJ. Effects of maternal protein restriction on the kidney of the newborn young of rats. *J Nutr* 1968;**94**(2):111-6.
192. Amri K, Freund N, Vilar J, Merlet-Benichou C, Lelievre-Pegorier M. Adverse effects of hyperglycemia on kidney development in rats: in vivo and in vitro studies. *Diabetes* 1999;**48**(11):2240-5.
193. Nathanson S, Moreau E, Merlet-Benichou C, Gilbert T. In utero and in vitro exposure to beta-lactams impair kidney development in the rat. *J Am Soc Nephrol* 2000;**11**(5):874-84.
194. Lelievre-Pegorier M, Vilar J, Ferrier ML, et al. Mild vitamin A deficiency leads to inborn nephron deficit in the rat. *Kidney Int* 1998;**54**(5):1455-62.
195. Merlet-Benichou C, Gilbert T, Muffat-Joly M, Lelievre-Pegorier M, Leroy B. Intrauterine growth retardation leads to a permanent nephron deficit in the rat. *Pediatr Nephrol* 1994;**8**(2):175-80.

196. Jones SE, Nyengaard JR, Flyvbjerg A, Bilous RW, Marshall SM. Birth weight has no influence on glomerular number and volume. *Pediatr Nephrol* 2001;16(4):340-5.
197. Manalich R, Reyes L, Herrera M, Melendi C, Fundora I. Relationship between weight at birth and the number and size of renal glomeruli in humans: a histo-morphometric study. *Kidney Int* 2000;58(2):770-3.
198. Merlet-Benichou C, Leroy B, Gilbert T. Intrauterine growth retardation and inborn nephron deficit. *Medecine/Sciences* 1993;9:777-780.
199. Bertram JF, Johnson K, Hughson MD, Hoy WE. Renal glomerular number and size in Australian Aborigines, African Americans and white populations from the same locations: a preliminary report. *Image Anal Stereol* 2001;20(Supplement 1):118-122.
200. Farris A, Hughson MD, Bertram JF, Hoy WE. Glomerular number and size in autopsy kidneys: relationship to birthweight (preliminary findings). *Lab Invest* 2002;82:1148A.
201. Rossing P, Tarnow L, Nielsen FS, Hansen BV, Brenner BM, Parving HH. Low birth weight. A risk factor for development of diabetic nephropathy? *Diabetes* 1995;44(12):1405-7.
202. Nelson RG, Morgenstern H, Bennett PH. Birth weight and renal disease in Pima Indians with type 2 diabetes mellitus. *Am J Epidemiol* 1998;148(7):650-6.
203. Zidar N, Cavic MA, Kenda RB, Koselj M, Ferluga D. Effect of intrauterine growth retardation on the clinical course and prognosis of IgA glomerulonephritis in children. *Nephron* 1998;79(1):28-32.
204. Yudkin JS, Phillips DI, Stanner S. Proteinuria and progressive renal disease: birth weight and microalbuminuria. *Nephrol Dial Transplant* 1997;12(Suppl 2):10-3.
205. Rowley KG, Iser DM, Best JD, O'Dea K, Leonard D, McDermott R. Albuminuria in Australian Aboriginal people: prevalence and associations with components of the metabolic syndrome. *Diabetologia* 2000;43(11):1397-403.
206. Guest CS, Ratnaike S, Larkins RG. Albuminuria in aborigines and Europids of south-eastern Australia. *Med J Aust* 1993;159(5):335-8.

207. Hoy WE, Wang Z, VanBuynder P, Baker PR, McDonald SM, Mathews JD. The natural history of renal disease in Australian Aborigines. Part 2. Albuminuria predicts natural death and renal failure. *Kidney Int* 2001;60(1):249-56.

208. Moore L, Lloyd MS, Pugsley DJ, Seymour AE. Renal disease in the Australian Aboriginal population: a pathological study. *Nephrology* 1996;2:315-321.

209. Cotran RS, Kumar V, Collins T. Robbins pathological basis of disease-- 6th ed. 6th ed. Philadelphia: W.B. Saunders Company, 1999.

210. Bertram JF, Young RJ, Seymour AE, Kincaid-Smith P, Hoy W. Glomerulomegaly in Australian Aborigines. *Nephrology* 1998;4:S46-S53.

211. Young RJ, Hoy WE, Kincaid-Smith P, Seymour AE, Bertram JF. Glomerular size and glomerulosclerosis in Australian aborigines. *Am J Kidney Dis* 2000;36(3):481-9.

212. Pesce CM, Schmidt K, Fogo A, et al. Glomerular size and the incidence of renal disease in African Americans and Caucasians. *Journal of Nephrology* 1994;7(6):355-358.

213. Abdi R, Slakey D, Kittur D, Racusen LC. Heterogeneity of glomerular size in normal donor kidneys: impact of race. *Am J Kidney Dis* 1998;32(1):43-6.

214. Hoy W, Bertram JF, Hughson MD, Cass A, Johnson K, Denton-Douglas R. A stereological study of glomerular number and size: a multiracial study of kidneys at autopsy. *Kidney Int* 2002;In press.

215. Wilcox AJ. On the importance--and the unimportance--of birthweight. *Int J Epidemiol* 2001;30(6):1233-41.

216. Joseph KS, Kramer MS. Review of the evidence on fetal and early childhood antecedents of adult chronic disease. *Epidemiol Rev* 1996;18(2):158-74.

217. Robinson WS. Ecological correlations and the behaviour of individuals. *American Sociological Review* 1950;15:351-357.

218. Macintyre S, Ellaway A. Ecological approaches: rediscovering the role of the physical and social environment. In: Berkman LF, Kawachi I, eds. Social epidemiology. Oxford: Oxford University Press, 2000: 332-348.

219. Bailie R, Siciliano F, Dane G, Bevan L, Paradies Y, Carson B. Atlas of health-related infrastructure in discrete Indigenous communities. Melbourne: The Aboriginal and Torres Strait Islander Commission National Housing and Infrastructure Centre, 2002.
220. Schwartz S, Susser E, Susser M. A future for epidemiology? *Annu Rev Public Health* 1999;20:15-33.
221. McMichael AJ. Prisoners of the proximate: loosening the constraints on epidemiology in an age of change. *Am J Epidemiol* 1999;149(10):887-97.
222. Marmot MG, Rose G, Shipley M, Hamilton PJ. Employment grade and coronary heart disease in British civil servants. *J Epidemiol Community Health* 1978;32(4):244-9.
223. Berkman LF, Kawachi I. Social epidemiology. New York ; Oxford: Oxford University Press, 2000.
224. Krieger N. Theories for social epidemiology in the 21st century: an ecosocial perspective. *Int J Epidemiol* 2001;30(4):668-77.
225. Brunner E, Marmot M. Social organization, stress and health. In: Marmot M, Wilkinson RG, eds. Social determinants of health. Oxford: Oxford University Press, 1999: 17-43.
226. McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med* 1998;338(3):171-9.
227. Lynch JW, Smith GD, Kaplan GA, House JS. Income inequality and mortality: importance to health of individual income, psychosocial environment, or material conditions. *Bmj* 2000;320(7243):1200-4.
228. Gulati PV, Singh KP, Braganza C. Role of sociocultural and environmental factors in the cause of scabies. *Int J Dermatol* 1977;16(4):281-3.
229. Landwehr D, Keita SM, Ponnighaus JM, Tounkara C. Epidemiologic aspects of scabies in Mali, Malawi, and Cambodia. *Int J Dermatol* 1998;37(8):588-90.
230. Currie BJ, Carapetis JR. Skin infections and infestations in Aboriginal communities in northern Australia. *Australas J Dermatol* 2000;41(3):139-43; quiz 144-5.

231. Streeton CL, Hanna JN, Messer RD, Merianos A. An epidemic of acute post-streptococcal glomerulonephritis among aboriginal children. *J Paediatr Child Health* 1995;**31**(3):245-8.
232. Goodfellow AM, Hoy WE, Sriprakash KS, Daly MJ, Reeve MP, Mathews JD. Proteinuria is associated with persistence of antibody to streptococcal M protein in Aboriginal Australians. *Epidemiol Infect* 1999;**122**(1):67-75.
233. Atkins RC. How bright is their future? Post-streptococcal glomerulonephritis in Indigenous communities in Australia. *Med J Aust* 2001;**174**(10):489-90.
234. White AV, Hoy WE, McCredie DA. Childhood post-streptococcal glomerulonephritis as a risk factor for chronic renal disease in later life. *Med J Aust* 2001;**174**(10):492-6.
235. Daniel M, O'Dea K, Rowley KG, McDermott R, Kelly S. Glycated hemoglobin as an indicator of social environmental stress among indigenous versus westernized populations. *Prev Med* 1999;**29**(5):405-13.
236. Devitt J, Tsey K, Hall G. An introduction to the social determinants of health in relation to the Northern Territory indigenous population. Casuarina: Cooperative Research Centre for Aboriginal and Tropical Health, 2001.
237. Wilson RD. Bringing them home : a guide to the findings and recommendations of the National Inquiry into the separation of Aboriginal and Torres Strait Islander children from their families. [Sydney]: Human Rights and Equal Opportunity Commission, 1997.
238. Schnall PL, Schwartz JE, Landsbergis PA, Warren K, Pickering TG. Relation between job strain, alcohol, and ambulatory blood pressure. *Hypertension* 1992;**19**(5):488-94.
239. Anderson NB, Myers HF, Pickering T, Jackson JS. Hypertension in blacks: psychosocial and biological perspectives. *J Hypertens* 1989;**7**(3):161-72.
240. Everson SA, Lynch JW, Chesney MA, et al. Interaction of workplace demands and cardiovascular reactivity in progression of carotid atherosclerosis: population based study. *Bmj* 1997;**314**(7080):553-8.
241. Cohen S, Doyle WJ, Skoner DP, Rabin BS, Gwaltney JM, Jr. Social ties and susceptibility to the common cold. *Jama* 1997;**277**(24):1940-4.

242. Ivers R. Indigenous Australians and tobacco: a literature review. Darwin: Cooperative Research Centre for Aboriginal and Tropical Health, 2001.
243. Ruggenenti P, Schieppati A, Remuzzi G. Progression, remission, regression of chronic renal diseases. *Lancet* 2001;**357**(9268):1601-8.
244. Muntner P, Coresh J, Smith JC, Eckfeldt J, Klag MJ. Plasma lipids and risk of developing renal dysfunction: the atherosclerosis risk in communities study. *Kidney Int* 2000;**58**(1):293-301.
245. Pinto-Sietsma SJ, Mulder J, Janssen WM, Hillege HL, de Zeeuw D, de Jong PE. Smoking is related to albuminuria and abnormal renal function in nondiabetic persons. *Ann Intern Med* 2000;**133**(8):585-91.
246. Ritz E, Ogata H, Orth SR. Smoking: a factor promoting onset and progression of diabetic nephropathy. *Diabetes Metab* 2000;**26 Suppl 4**:54-63.
247. Orth SR, Stockmann A, Conradt C, et al. Smoking as a risk factor for end-stage renal failure in men with primary renal disease. *Kidney Int* 1998;**54**(3):926-31.
248. Celermajer DS, Sorensen KE, Georgakopoulos D, et al. Cigarette smoking is associated with dose-related and potentially reversible impairment of endothelium-dependent dilation in healthy young adults. *Circulation* 1993;**88**(5 Pt 1):2149-55.
249. Celermajer DS, Adams MR, Clarkson P, et al. Passive smoking and impaired endothelium-dependent arterial dilatation in healthy young adults. *N Engl J Med* 1996;**334**(3):150-4.
250. Benigni A, Remuzzi G. Mechanism of progression of renal disease: growth factors and related mechanisms. *J Hypertens Suppl* 1998;**16**(4):S9-12.
251. Oikawa T, Freeman M, Lo W, Vaughan DE, Fogo A. Modulation of plasminogen activator inhibitor-1 in vivo: a new mechanism for the anti-fibrotic effect of renin-angiotensin inhibition. *Kidney Int* 1997;**51**(1):164-72.
252. Plunkett A, Lancaster P, Huang J, National Perinatal Statistics Unit (Australia). Indigenous mothers and their babies Australia 1991-1993. Sydney: AIHW National Perinatal Statistics Unit, 1996.
253. de Costa C, Child A. Pregnancy outcomes in urban aboriginal women. *Med J Aust* 1996;**164**(9):523-6.

254. Wong LC, Amega B, Connors C, et al. Outcome of an interventional program for scabies in an Indigenous community. *Med J Aust* 2001;175(7):367-70.
255. Hoy WE, Baker PR, Kelly AM, Wang Z. Reducing premature death and renal failure in Australian aboriginals. A community-based cardiovascular and renal protective program. *Med J Aust* 2000;172(10):473-8.
256. Cass A, Cunningham J, Snelling P, Wang Z, Hoy W. Urban disadvantage and delayed nephrology referral in Australia. *Health and Place* 2002;In press.
257. Cass A, Cunningham J, Snelling P, Wang Z, Hoy W. Renal transplantation in Aboriginal Australians: access, timing and outcomes. *Journal of American Society of Nephrology* 2001;12:881A.
258. Cass A, Lowell A, Christie M, et al. Sharing the true stories: improving communication between Aboriginal patients and healthcare workers. *MJA* 2002;176(10):466-470.
259. Mackerras D. Evaluation of the Strong Women, Strong Babies, Strong Culture Program : results for the period 1990-1996 in three pilot communities. Darwin: Menzies School of Health Research, 1998.
260. Pholeros P, Rainow S, Torzillo PJ. Housing for health - towards a healthier living environment for Aborigines. Sydney: HealthHabitat, 1994.
261. Fried LF, Orchard TJ, Kasiske BL. Effect of lipid reduction on the progression of renal disease: a meta-analysis. *Kidney Int* 2001;59(1):260-9.

APPENDICES

APPENDIX 1: KIDNEY DISEASE: ARE YOU AT RISK?

Screening of selected patients for proteinuria could help reduce the incidence of end-stage renal disease

Publication details:

Cass A. Kidney disease: are you at risk? (Editorial) *Medical Journal of Australia* 2002; 176 (11): 515-516.

Introduction

In 2000, chronic or unspecified renal failure was listed as a cause of death of 9,160 Australians (7.1% of all deaths) (source: Australian Bureau of Statistics, special data request, 2002). Most would have had chronic renal impairment (CRI) for years. Each year, more than 1,700 people with end-stage renal disease (ESRD) start dialysis or receive a transplant.[1] These figures suggest that the impact of CRI is substantial and that in order to prevent progression to ESRD we need to develop systems for its detection and management.

Prevalence and significance of proteinuria

The Australian Diabetes, Obesity and Lifestyle (AUSDIAB) study,[2] a cross-sectional survey of a sample of over 11,000 Australians aged 25 and over, found proteinuria in 2.5% of the study population and serum creatinine level above 120µmol/L in 1.1% (reference range, 50-110µmol/L (adult women), 60-120µmol/L (adult men)). A recent US study estimated that 1.5% of people aged six years and over have proteinuria.[3] Extrapolating from these data, it is likely that several hundred thousand Australians have proteinuria, which is associated with a 15-fold increased risk of developing ESRD within 10 years.[4]

Whose urine should be screened?

Current evidence does not support universal screening for proteinuria. The US Multiple Risk Factor Intervention Trial,[5] in which more than 300,000 men were screened and followed up for an average of 16 years, showed that older age, smoking, hypertension and diabetes were significant risk factors for ESRD. Familial aggregation of ESRD, in excess of that predicted by clustering of diabetes and hypertension, has also been demonstrated.[6] Indigenous Australians, who make up less than 2% of our population, comprise more than 8% of ESRD patients;[1] and, in some remote communities where screening has been conducted, almost 25% of adults have been found to have proteinuria.[7] Specific groups of people known to be at increased risk of ESRD should therefore be targeted for screening (see Box 1).

Dipstick testing is cheap (about $0.50 per test), with immediate results. More than a trace of protein indicates a protein excretion rate greater than 300mg in 24 hours. In the AUSDIAB study,[2] dipstick testing had about 85% sensitivity and specificity (S.Chadban, Nephrologist, AUSDIAB Steering Committee, personal communication). As about 15% of people *without* proteinuria have a falsely positive result, people with a positive dipstick result should have their protein excretion rate quantified by further testing. Measurement of 24-hour urinary protein has long been the gold standard, but reliable collection is often impractical. Measurement of the albumin-creatinine ratio (ACR) in a morning urine specimen is easier and sufficiently precise.[8] An ACR over 34g/mol indicates a daily protein excretion rate exceeding 300mg. At the same time as measuring the urinary ACR, a blood sample should be sent for measurement of serum creatinine and electrolyte levels for further assessment of renal function.

Most dipsticks also test the urine for substances other than protein. If leucocytes or nitrites are detected, especially with symptoms suggestive of a urinary tract infection, a mid-stream urine specimen should be cultured. The dipstick test for protein should be repeated after treatment of any infection. Isolated haematuria rarely indicates glomerular pathology associated with progressive renal disease. However, among smokers and those screened on the basis of age, a finding of haematuria should prompt exclusion of urinary tract malignancy.

Interpreting the serum creatinine

Serum creatinine level per se is not an accurate indicator of renal function. The glomerular filtration rate (GFR), which can be estimated from the serum creatinine level, is the most meaningful single measure (see Box 2). In healthy adults, the GFR exceeds 80mL/min; patients with a GFR between 30 and 80mL/min have CRI; while a GFR below 30mL/min indicates severe impairment with a high risk of progression to ESRD, warranting prompt referral to a nephrologist.

Managing CRI in general practice

General practitioners can substantially reduce the risk of progression of renal impairment. Management guidelines developed by the Australian Kidney Foundation and the Australia and New Zealand Society of Nephrology are accessible at the "Caring for Australians with Renal Impairment" web-site.[9] I discuss here the evidence for the interventions recommended in the guidelines. Further benefit may be obtained from reducing the high risk of cardiovascular events that accompanies renal disease.[10]

Intensive control of hyperglycaemia and hypertension is beneficial in people with diabetes. (Specific interventions for diabetes are beyond the scope of this article – see the guidelines of the Australian Diabetes Society, available at http://www.racp.edu.au/ads.)

In all patients with CRI, management aims should be the reduction of proteinuria (to ACR <100g/mol) and the maintenance of renal function (i.e. stable GFR). These can be achieved through intensive control of hypertension[9] (Level I evidence[11]). Suggested blood-pressure targets are 125/75mmHg (in people under 50) and 135/85mmHg (in people ≥ 50 years). Multi-drug therapy is usually required. Angiotensin converting enzyme inhibitors and angiotensin-II receptor antagonists have been shown to be reno-protective (Level I and Level II evidence respectively).[9] Even in the absence of hypertension, they may be effective in people with protein excretion exceeding 1g/day (an ACR above 100g/mol). Treatment for this normotensive group should be adjusted according to the level of proteinuria and monitored with three monthly to six monthly ACR estimates. Potential risks include hyperkalaemia and, in patients with renal artery stenosis, worsening of renal impairment. In randomised, controlled trials of these agents, participant drop-out rates due to adverse effects have been low.

Because smoking is associated with a greater risk of progression (Level III-2 evidence),[9] smokers should be assisted to quit smoking. A low protein diet is not recommended, as the benefit is minimal and malnutrition may ensue. There

is little evidence regarding the impact of exercise; however, in view of its cardiorespiratory benefits, regular exercise is advised. There is currently insufficient evidence to warrant lipid-lowering therapy as a means of minimising progression.

Who should be referred to a nephrologist?

GPs can usually manage patients with CRI, preventing further renal damage and progression to renal failure. Indications for prompt referral to a nephrologist include:

- estimated GFR below 30 mL/min;
- estimated GFR above 30 mL/min, but declining rapidly;
- age less than 35;
- ACR greater than 300g/mol (nephrotic range for proteinuria);
- symptoms or signs suggestive of systemic illness (e.g systemic lupus erythematosis); or
- failure to reach blood pressure or ACR targets within six months of starting antihypertensive drug therapy.

Box 1

Indications for annual dipstick testing for proteinuria:

Age over 50

Hypertension

Smoking

Diabetes*

Family history of renal disease

Aboriginal or Torres Strait Islander descent

*People with diabetes also require annual testing for microalbuminuria. (See the Australian Diabetes Society Position Statement 'Microalbuminuria in Diabetes' (p4) at http://www.racp.edu.au/ads/posstate.htm)

Box 2

Calculation of glomerular filtration rate (GFR) by the modified Cockcroft-Gault formula*:[12]

For women:

Estimated GFR (in mL/min)† = (140-age (in years)) x weight (in kg) / serum creatinine level (in µmol/L)

For men:

Calculate estimated GFR as for women, then multiply by 1.23.

*The modification is an arithmetic simplification of the original formula. The GFR estimate obtained will be 4% lower for women, and unchanged for men, compared to an estimate obtained using the original formula.

†A number of computerized clinical record systems include a calculator for this formula.

References

1. Russ GR, ed. ANZDATA Registry Report 2001. Adelaide: Australia and New Zealand Dialysis and Transplant Registry, 2002.

2. Australian Diabetes Obesity and Lifestyle Study, Dunstan DW, International Diabetes Institute. Diabesity & associated disorders in Australia - 2000: the accelerating epidemic. Melbourne: International Diabetes Institute, 2001.

3. Jones CA, Francis ME, Eberhardt MS, et al. Microalbuminuria in the US population: third National Health and Nutrition Examination Survey. *Am J Kidney Dis* 2002;**39**(3):445-59.

4. Iseki K, Iseki C, Ikemiya Y, Fukiyama K. Risk of developing end-stage renal disease in a cohort of mass screening. *Kidney Int* 1996;**49**(3):800-5.

5. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Stamler J. End-stage renal disease in African-American and white men. 16-year MRFIT findings. *Jama* 1997;**277**(16):1293-8.

6. Lei HH, Perneger TV, Klag MJ, Whelton PK, Coresh J. Familial aggregation of renal disease in a population-based case-control study. *J Am Soc Nephrol* 1998;**9**(7):1270-6.

7. Hoy WE, Mathews JD, McCredie DA, et al. The multidimensional nature of renal disease: rates and associations of albuminuria in an Australian Aboriginal community. *Kidney Int* 1998;**54**(4):1296-304.

8. Ruggenenti P, Gaspari F, Perna A, Remuzzi G. Cross sectional longitudinal study of spot morning urine protein:creatinine ratio, 24 hour urine protein excretion rate, glomerular filtration rate, and end stage renal failure in chronic renal disease in patients without diabetes [published erratum appears in BMJ 1998 Nov 28;317(7171):1491]. *BMJ* 1998;**316**(7130):504-9.

9. Australian Kidney Foundation & Australia New Zealand Society of Nephrology. The CARI Guidelines (Caring for Australians with Renal Impairment). 2001.

10. Baigent C, Burbury K, Wheeler D. Premature cardiovascular disease in chronic renal failure. *Lancet* 2000;**356**(9224):147-52.

11. National Health and Medical Research Council. How to use evidence: assessment and application of scientific evidence. Canberra: National Health and Medical Research Council, 2000.

12. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976;**16**(1):31-41.

APPENDIX 2: EARLY RENAL IMPAIRMENT: THE ROLE OF THE GENERAL PRACTITIONER

Publication details:

Usherwood T, Cass A. Early renal impairment: the role of the general practitioner. *Medicine Today*. In press.

In summary

- Patients at risk of early renal impairment should be offered annual screening for proteinuria.
- Renal function can be estimated from serum creatinine using the modified Cockcroft-Gault formula.
- Patients with early renal impairment should be advised to stop smoking, take regular exercise, and maintain a normal protein intake.
- Non-steroidal anti-inflammatory drugs and COX-2 inhibitors should be avoided in early renal impairment. ACE inhibitors, angiotensin II receptor antagonists, diuretics and radiological contrast agents should be prescribed with care.
- Strict control of blood pressure and careful management of proteinuria, diabetes and anaemia improve outcomes for patients with early renal impairment.
- Patients with *severe* renal impairment should be referred promptly to a nephrologist. Referral should also be considered for younger patients, or if renal function is declining rapidly, if proteinuria is heavy, there is significant comorbidity or if treatment targets prove difficult to achieve.

Introduction

Approximately 1,500 people develop end-stage renal disease (ESRD) each year in Australia. Most will have had early renal impairment (ERI) for many years. Appropriate treatment could have slowed or prevented their progression to ESRD. In this article we outline the epidemiology of ERI in Australia, identify the known risk factors, and describe an evidence-based approach to its detection and management in general practice. We have based this article on the research evidence summarized in the websites listed under 'Useful resources' and on other authoritative sources.

Epidemiology of early renal impairment

The AUSDIAB study, a cross-sectional survey of a representative sample of over 11,000 Australian adults aged 25 years or over, found that 2.5% had proteinuria and 1.1% had a serum creatinine of over 120µmol/L. This implies that several hundred thousand Australians have significant ERI. In rural and remote Aboriginal communities, almost 25% of adults have proteinuria. Japanese studies indicate that people with proteinuria are 15 times more likely than people without proteinuria to develop ESRD within ten years.

A number of risk factors have been identified for ERI (see Box 1). Indigenous Australians constitute less than 2% of the population but almost 10% of patients commencing treatment for ESRD. A family history features in most of the leading causes of ESRD including diabetes, familial types of glomerulonephritis, hypertension and polycystic kidney disease. In the Multiple Risk Factor Intervention Trial (MRFIT study) in the USA, over 300,000 men were screened and followed-up for an average of 16 years. Older age, smoking, hypertension and diabetes were major risk factors for ESRD.

Urine testing - who should be screened?

The best single screening test for ERI is dipstick testing for proteinuria. It is cheap and there is an immediate result. There is a strong correlation between

raised urinary protein excretion and progression towards renal failure. Furthermore, interventions that slow the progress of renal disease seem to be most effective in those patients with the worst proteinuria.

Although universal population screening for proteinuria is not currently considered worthwhile, all patients with one or more risk factors for ERI should be offered annual dipstick testing. Dipstick testing for proteinuria is, however, inadequate for people with diabetes; they require their urinary albumin excretion rate to be measured at least annually.

Dipstick positive - what next?

Dipstick testing has a specificity of about 85% in detecting proteinuria (urinary protein excretion greater than 300mg in 24 hours). This means that the test will be falsely positive in approximately 15% of people who don't have proteinuria. It is important therefore, to check by quantifying the protein excretion in any patient whose dipstick test is positive.

The gold standard is measurement of the total amount of protein in a 24-hour urine specimen. However, reliable collection of the complete specimen is often impractical. An easier alternative, with excellent precision, is measurement of the albumin-creatinine ratio (ACR) in an early morning urine specimen. (See Box 2 for interpretation of ACR results.) At the same time, the patient's blood pressure should be checked (if this hasn't been done already), and blood should be sent for measurement of serum levels of urea, creatinine and electrolytes.

Most dipsticks also test the urine for substances other than protein. If other abnormalities are detected, then they should be followed up appropriately. If leucocytes or nitrites are detected, a mid-stream specimen should be obtained for culture. The dipstick test for protein should be repeated after treatment of any infection. The presence of blood in the urine is always an abnormal finding, and should lead to appropriate investigation and referral.

The sensitivity of dipstick testing for proteinuria is about 80%. This means that approximately 20% of people who do, in fact, have proteinuria will have a false-negative dipstick test. Therefore, people with the risk factors listed in Box 1 should be tested annually, and any modifiable risk factors (hypertension, diabetes and smoking) should be managed appropriately.

Interpreting the serum creatinine

The single most meaningful measure of renal function is the glomerular filtration rate (GFR). Its direct measurement is inconvenient, but GFR can be estimated from the serum creatinine, using the modified Cockcroft-Gault formula (Box 3). This formula utilizes the patient's creatinine level, age, weight and sex. A number of computerized clinical record systems include a calculator for the Cockcroft-Gault formula. It is important to note that a patient with a normal serum creatinine concentration can still have significant renal impairment (see Box 4), so:

"Think GFR, not serum creatinine"

The normal range for GFR in adults is over 80 mls/min. Patients whose GFR is reduced, but is greater than 30 ml/min, are said to have ERI. Patients with GFR less than 30 ml/min have severe renal impairment, are at high risk of progression to end-stage renal disease, and should be referred promptly to a nephrologist.

The Cockcroft-Gault formula does not always give an accurate estimate of GFR in patients with severe renal impairment, decompensated cirrhosis, cancer, or obesity. Clinically important errors can arise in patients with these conditions (see Box 5).

The management of ERI in general practice

Patients with ERI are at risk of progression to end-stage disease, but this risk can be substantially reduced by appropriate management by their general practitioner. Key aspects of the management of ERI are listed in Box 6, and are described in more detail below.

Stop smoking

Smokers with renal disease progress to renal failure more rapidly than non-smokers. In addition to many other health benefits, stopping smoking slows the rate of progression, at least in diabetic renal disease. Smokers with ERI should be encouraged to stop, and assisted to do so.

Drugs to watch

A number of commonly prescribed medications may exacerbate renal impairment. Non-steroidal anti-inflammatory drugs (NSAIDs) and COX-2 inhibitors should, if at all possible, be avoided. Although ACE inhibitors, angiotensin II receptor (AIIR) antagonists and diuretics are key medications in the management of progressive renal disease, hypertension and heart disease, their use must be carefully monitored as they may exacerbate renal impairment in certain situations. Radiologists should be alerted to patients with renal impairment, so that they can use appropriate preventive strategies when the use of contrast agents is indicated.

No protein restriction

Traditionally, patients with renal disease were recommended a low-protein diet. However, the impact on progression was minimal, while many became malnourished. Patients with renal impairment should consume the normal recommended daily intake of 0.75 - 1.0 g protein per kg.

Exercise

Exercise does not appear to slow the progress of renal insufficiency, but the evidence on this point is weak. Given its other benefits, patients with ERI should be advised to take regular exercise.

Immunization

The NHMRC currently recommends annual influenza immunization for patients with diabetes, renal dysfunction or other chronic illness requiring regular medical follow-up. Pneumococcal vaccination is also recommended for patients with diabetes or chronic renal disease.

Strict control of blood pressure

Strict control of blood pressure slows the progression of renal impairment, in addition to reducing cardiac and cerebrovascular complications. The blood pressure targets currently recommended for patients with ERI are below 120/75 mmHg for patients under 50 years of age, and below 130/85 mmHg for those over 50. Achieving these targets usually requires the use of more than one antihypertensive drug.

Angiotensin converting enzyme (ACE) inhibitors are particularly effective in protecting renal function. They can usually be started in general practice, as they are generally safe and well tolerated. Potential risks are first-dose hypotension, hyperkalaemia, and worsening of renal impairment in patients with renal artery stenosis. However, in randomised, controlled trials of ACE inhibitors against placebo, drop-out rates due to adverse effects have been extremely low.

First dose hypotension is a potential risk in patients who are hypovolaemic (eg due to diuretic treatment), who have severe hypertension, or who are elderly. The initial dose should be low for all patients, especially for the elderly, and diuretics should, if possible, be withheld for 2-3 days before commencing

therapy. If this is not possible, the patient may require hospitalization to start treatment.

The patient's serum potassium should be known before an ACE inhibitor is prescribed. The serum potassium, urea and creatinine should be checked about seven days later and again at four and eight weeks. A rise in serum creatinine of greater than 30% above baseline within the first two months of commencing treatment is considered significant, and the patient should be advised to stop the ACE inhibitor immediately.

Angiotensin II receptor (AIIR) antagonists are appropriate alternatives for patients who cannot tolerate an ACE inhibitor because of troublesome cough or other side-effect. This class of drugs also has reno-protective properties. However, like ACE inhibitors, they can cause both hyperkalaemia and deterioration in renal function.

Non-dihydropyridine calcium antagonists such as diltiazem or verapamil, which also have reno-protective properties, may be prescribed for patients who can tolerate neither an ACE inhibitor nor an AIIR antagonist.

Most patients with ERI will not achieve target blood pressures despite taking the maximum recommended dose of a single agent. Possible reasons that should be considered include 'white coat hypertension', inappropriate sphygmomanometer cuff size, poor compliance with therapy, high salt intake, heavy alcohol consumption, or intake of medication that exacerbates hypertension, such as an NSAID. If these factors are excluded, then a second drug is needed. For patients taking an ACE inhibitor or AIIR antagonist, the addition of a non-dihydropyridine calcium antagonist, a beta-blocker or a non-potassium sparing diuretic may be appropriate. A patient taking diltiazem may be prescribed a beta-blocker, but the combination of a beta-blocker with verapamil can be dangerous and should be avoided.

Treatment of proteinuria

Not all patients with ERI have raised blood pressure. However, both ACE inhibitors and AIIR antagonists slow the progress of renal impairment in patients with proteinuria, even in the absence of hypertension. Intervention is beneficial for people with proteinuria of more than 1g/day, which is equivalent to an ACR of more than 100 g/mol. Therefore a drug in one of these classes should be considered for any patient with early renal impairment and proteinuria, irrespective of their blood pressure. The initial dosage should be low and subsequently increased as tolerated. Used in this manner, treatment should not cause symptomatic hypotension. In non-diabetics, the treatment should be titrated against the level of proteinuria, with the aim of reducing protein excretion to less than 1g per day (urine ACR of less than 100g/mol).

Renal damage in diabetes

One of the first clinical indicators of renal damage in both Type 1 and Type 2 diabetes is microalbuminuria (24-hour albumin excretion 30 - 300 mg). Therefore, patients with diabetes should be treated at much lower levels of albumin excretion than other at-risk patients. An ACE inhibitor or AIIR antagonist should be prescribed for any patient with diabetes and *either* micro- *or* macro-albuminuria. These classes of drug are also the first choice for control of high blood pressure, even if urinary protein excretion is normal. On present evidence, patients with diabetes who have neither hypertension nor microalbuminuria should not routinely be prescribed one of these drugs.

Control of hyperglycaemia is also important in slowing the progress of renal disease. The currently recommended targets are pre-prandial blood glucose concentrations 4.4 - 6.7 mmol/l, and glycosylated haemoglobin (HbA1c) less than 7%.

Anaemia

Anemia may be a consequence of chronic renal impairment and often develops early in the course of ERI. Once other causes have been excluded, iron and/or

erythropoietin therapy to achieve a haemoglobin of above 10g/dl enhances quality of life, reduces breathlessness and lethargy, and improves exercise tolerance. Referral to a hospital-based specialist, usually a nephrologist, is necessary to commence erythropoeitin therapy.

Working with the patient

Most of the work of managing renal disease is done by the patient and their family. We have not found any studies relating specifically to ERI, but research has clearly demonstrated the importance of four elements of health care in helping patients manage chronic illness:

- Collaborative problem definition. The patient and their doctor need to develop a shared appreciation of the problems and issues to be addressed. It is the responsibility of the doctor to explain relevant aspects of what is known about ERI and its management, and to explore with the patient their understanding, concerns, preferences and expectations of care.
- Prioritizing, goal setting and planning. The doctor should work with the patient in identifying the issues of greatest importance to each of them, in setting achievable goals (for example, to stop smoking or to control hyperglycaemia), and in developing a realistic action plan to address these goals.
- Education and support. Patients and their families need information about ERI and its treatment, help in lifestyle modification, and support in coping with the emotional demands and practical implications.
- Active and sustained follow-up. Patients with ERI should be seen regularly in the practice, preferably by the same doctor each time, and attempts should be made to contact patients who miss their appointment.

Indications for referral

Patients with a GFR of less than 30 ml/min should be referred promptly to a nephrologist. Referral should also be considered for patients aged less than 35

years, patients whose GFR is above 30 ml/min but declining rapidly, patients who have proteinuria of more than 3 grams per day, and patients who have significant co-morbid illness or evidence of a systemic disease such as SLE. Referral should also be considered for patients who do not reach targets for blood pressure or protein excretion within six months (see Box 8).

Risk-based management

Traditionally, patients with signs of organ dysfunction are offered investigation to ascertain the causative pathology, to assess the severity of the disease process and to guide appropriate therapy. There is no evidence, however, that all patients gain net benefit from intensive investigation of ERI. Instead, the evidence supports the paradigm illustrated in Box 9. Investigation of the patient at risk is aimed primarily at stratification: patients at high risk of progress towards ESRD should be referred to a nephrologist for further investigation (see Box 8). Patients at low risk can be managed in general practice, with the aim of preventing further renal damage and avoiding progression to renal failure.

Useful Resources

CARI guidelines: Caring for Australians with Renal Impairment
http://www.cari.kidney.org.au/

New Zealand Guidelines Group: Primary care guidelines for the management of core aspects of diabetes
http://www.nzgg.org.nz/library/gl_complete/diabetes/index.cfm#contents

National Heart Foundation of Australia: Guide to management of hypertension
http://www.heartfoundation.com.au/

Box 1

Risk factors for ERI in Australia

Aboriginal or Torres Strait Islander
Aged 50 years or over
Diabetes mellitus
Family history of renal disease
High blood pressure
Smoker

Patients with one or more of the risk factors should be offered annual dipstick testing for proteinuria. However, this is inadequate for patients with diabetes, who should have their urinary albumin excretion rate measured at least annually.

Box 2

Interpretation of urinary albumin-creatinine ratios (ACR)

ACR (g/mol)	Daily protein excretion	Nomenclature
< 3.4	< 30 mg	Normal
3.4 to 34	30 to 300 mg	Microalbuminuria
> 34	> 300 mg	Proteinuria
> 300	>3 g	Proteinuria - nephrotic

Urinary albumin is in mg/L
Urinary creatinine is in mmol/L

Box 3

The modified Cockcroft-Gault formula

For women:
Estimated GFR = (140-age) x weight / serum creatinine

For men:
Calculate estimated GFR as for women, then multiply by 1.23

GFR is expressed as ml/min
Age is in years
Weight is in kilograms
Serum creatinine is in μmol/L

Note. The modification is an arithmetic simplification of the original formula. The GFR estimate obtained will be 4% lower for women and unchanged for men, compared with an estimate obtained using the original formula.

Box 4

"Think GFR, not serum creatinine"

Ms A.T. is aged 58 years and weighs 55 kg. Her serum creatinine is 107 μmol/L, which is within the laboratory's stated normal range of 60-120 μmol/L. However, her GFR, as estimated by the modified Cockcroft-Gault formula, is:

$$(140 - 58) \times 55 / 107 = 42 \text{ ml/min.}$$

Ms A.T. has significant renal impairment.

Box 5

When the Cockcroft-Gault formula may get it wrong

The formula will overestimate GFR if the patient is obese, has decompensated cirrhosis or has severe renal impairment (i.e. GFR < 30 ml/min).

The formula may underestimate GFR if the patient has cancer.

Box 6

Summary of management of early renal impairment in general practice

Address smoking
Avoid NSAIDs and COX-2 inhibitors
Advise normal protein intake
Recommend regular exercise
Consider immunization requirements
Treat hypertension
Treat proteinuria
Consider ACE inhibitor or AIIR antagonist
Manage diabetes
Address anaemia

Box 7

Commonly prescribed drugs that may worsen renal impairment

NSAIDs
COX-2 inhibitors
Diuretics
ACE inhibitors and AIIR antagonists
Contrast agents

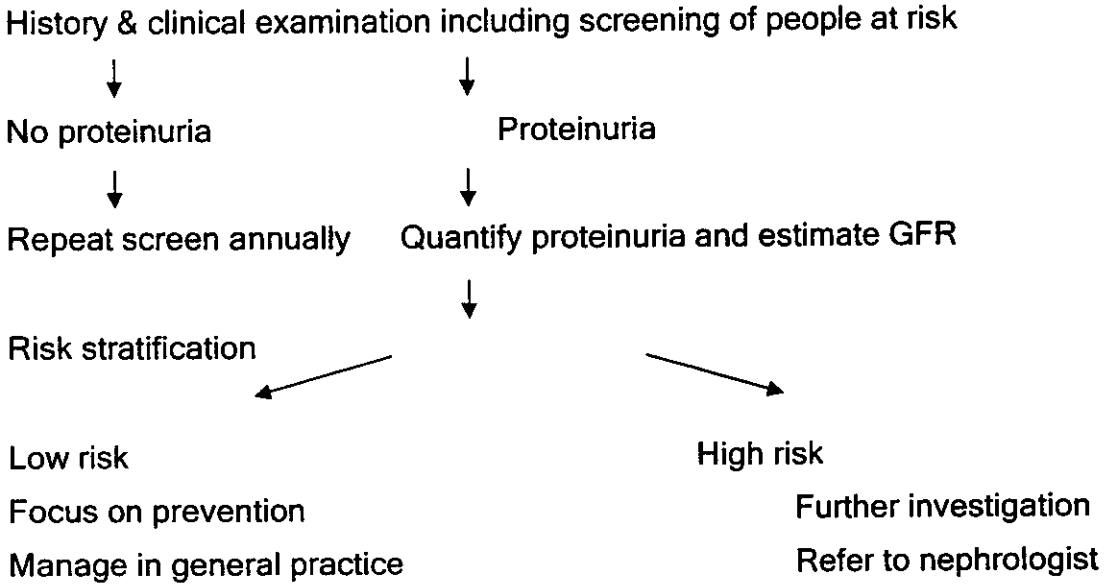
Box 8

When to consider referral to a nephrologist

Age less than 35 years
Estimated GFR less than 30 ml/min
GFR greater than 30 ml/min but declining rapidly
Nephrotic-range proteinuria (greater than 3g/24 hours)
Haematuria present
Significant co-morbidity or systemic illness
Anaemia due to renal impairment
Failure to reach targets for blood pressure or protein excretion within six months

Box 9

Risk-based management



APPENDIX 3: RENAL-RELATED DEATHS IN AUSTRALIA, 1997-1999

Publication details:

Li SQ, Cunningham J, Cass A. Renal-related deaths in Australia, 1997-1999. Submitted August 2002 *American Journal of Kidney Disease*.

Abstract

Background: Despite marked increases in cases of treated end-stage renal disease in Australia, little is known about renal disease mortality.

Aims: To quantify the contribution of renal diseases to mortality in Australia.

Methods: We examined data from the Australian Bureau of Statistics on underlying and associated causes of death (based on death certificates) for deaths occurring in 1997-99 and registered by the end of 1999. Causes of death were coded according to the International Classification of Diseases, 10th Revision (ICD-10). We included as renal a number of causes outside the ICD-10 chapter on diseases of the genito-urinary system (e.g. diabetic renal disease, hypertensive renal disease and congenital malformations of the kidney).

Results: Of 378,832 recorded deaths, renal disease was coded as the underlying cause for 7,888 (2.1%), and as an associated cause for another 28,012 (7.4 %). Among deaths with renal disease as the underlying cause, almost one in four (23.1%) were outside the ICD-10 genito-urinary chapter and therefore unlikely to be classified as a renal death in official statistics.

Conclusion: The contribution of renal disease to Australian mortality has been underestimated due to historical reliance on a single (underlying) cause of death and because the coding of many renal deaths places them outside the category typically included as renal in official mortality statistics.

Introduction

Between 1990 and 2000, the number of cases of treated end-stage renal disease in Australia increased by 83%, from 6,218 to 11,397 (Australia and New Zealand Dialysis and Transplant Registry, special data request, 2001). However, little is known about the contribution of renal disease to mortality. The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) reports on cause of death of patients with treated end stage renal disease.[1] ANZDATA reports do not include people with renal disease who have never received renal replacement therapy.

Recent Australian Bureau of Statistics (ABS) publications include figures for all diseases of the genito-urinary system combined (which includes non-renal conditions) and for certain types of renal failure.[2] Other important renal diseases, such as hypertensive or diabetic renal disease and congenital malformations (including polycystic kidney disease and vesico-ureteric reflux) can not be identified from published ABS data. These diseases represented four of the five commonest causes of treated end-stage renal disease in 2000.[1] Furthermore, ABS statistics have, until recently, been based on a single 'underlying' cause of death. This approach fails to reflect the complexity of death resulting from multiple chronic diseases, a phenomenon which has become increasingly common throughout most of the world.[3]

This study provides the first comprehensive assessment of the contribution made by renal disease to mortality in Australia. It includes an expanded classification of renal disease and uses multiple cause of death coding, as introduced by the ABS in 1997.

Methods

Data source

Data were obtained from the Australian Bureau of Statistics (ABS) for all deaths occurring in 1997-99 and registered by the end of 1999. This data set is based on death certificates provided by the State and Territory Registrars, with additional coding performed by the ABS.

The ABS data set included information on the underlying cause of death, up to twelve other conditions listed on the death certificate, and the age, sex, place of residence, and Indigenous status of the deceased. All diseases and conditions recorded on the death certificate had been coded by the ABS according to the International Classification of Diseases, 10th Revision (ICD-10).[4] The underlying cause of death was defined as 'the disease or injury which initiated the train of morbid events leading directly to death'.[2] The ABS uses the term 'multiple causes of death' to refer to all morbid conditions listed on the death certificate. These can include 'the underlying cause, the immediate cause, or any intervening causes and those conditions which contributed to death, but were not related to the disease or condition causing death'.[2] In order to distinguish between the underlying cause and other diseases and conditions listed, we used the term 'associated cause' to refer to diseases and conditions other than the underlying cause. Thus, for the purposes of this analysis, 'underlying causes' and 'associated causes' were mutually exclusive.

Definition of renal deaths

We defined renal causes to include diseases of the kidney and ureter (ICD-10 codes N00-N29), diabetic renal disease (E10.2, E11.2, E13.2 and E14.2), hypertensive renal disease (I12, I13, I15.0, I15.1) and congenital malformations of the kidney and ureter (Q60-Q63). We further sub-divided renal causes into 'renal failure' and 'other renal disease', as shown in Table 1.

It is possible to have one renal disease as the underlying cause and another as an associated cause. In order to avoid double-counting, we divided renal deaths into two mutually exclusive groups: deaths in which renal disease was the underlying cause, regardless of any associated causes; and deaths in which renal disease was not the underlying cause, but was listed as at least one of the associated causes.

Ethical approval

We obtained approval for the study from the Joint Institutional Ethics Committee of the Royal Darwin Hospital and the Menzies School of Health Research, and from the Northern Territory University Ethics Committee.

Results

Of the 378,882 deaths analysed, renal disease was listed as the underlying cause of death for 7,888 (2.1%). For an additional 28,012 (7.4 % of all deaths), renal disease was recorded as an associated cause. Thus approximately one in ten death certificates (9.5%) listed renal disease as a cause of death.

Of deaths with renal disease listed as the underlying cause, 1,824 (23.1%) were due to hypertensive renal disease, diabetic renal disease, or congenital malformations of the kidney (Table 1). As these diseases are not included in the ICD-10 as diseases of the genito-urinary system (ICD-10 codes N00-N99), routinely published official statistics are unlikely to identify deaths from these causes as renal deaths.

Renal disease as the underlying cause of death

The proportion of deaths with renal disease as the underlying cause increased with age. It varied by place of residence, sex and whether or not the deceased was recorded as being of Indigenous origin (Table 2). It was not common for renal disease to be reported alone: only 591 death certificates recorded renal disease as the underlying cause without any other causes. When renal disease was the underlying cause of death, there were an average of 2.5 additional causes of death. The most commonly mentioned associated causes were diseases of the circulatory system (33.7% of those mentioned; Table 3), followed by diseases of the respiratory system (14.4%) and the genito-urinary system (14.2%).

Renal disease as an associated cause of death

Renal disease was 3.6 times more likely to be reported as an associated cause of death than as the underlying cause of death. Among deaths with renal disease as an associated cause of death, the majority (65.2%) had, as the underlying cause, either a disease of the circulatory system or a neoplasm (Table 4).

For the 28,012 deaths for which renal disease was an associated cause, 887 (3.2%) death certificates made no mention of any diseases included in the ICD-10 chapter on genito-urinary system. These deaths, for which the relevant renal disease was hypertensive renal failure, hypertensive renal disease, diabetic renal disease, and/or congenital malformations of the kidney and ureter, are likely to be overlooked as renal-related deaths, even when multiple cause coding is used.

Renal disease in combination with other causes of death

Renal disease, whether the underlying or an associated cause, was commonly reported in combination with other chronic and acute diseases (Table 5). The majority (71%) of all renal-related death certificates listed at least one cardiovascular disease, with ischaemic heart disease appearing in about a third (33%). Respiratory disease (32%), neoplasms (20%), infectious and parasitic diseases (14%) and diabetes (14%) were also commonly reported as being associated with renal disease. The combination of renal disease, cardiovascular disease and diabetes was listed in more than one in every hundred death certificates.

Discussion

This study highlights the importance of renal disease as a cause of death. Approximately one in ten people who died in 1997-99 had a renal disease listed on their death certificates. The contribution of renal disease to Australian mortality has previously been underestimated due to two factors: the historical reliance on a single (underlying) cause of death and the coding of many renal deaths outside the category typically included as renal in official mortality statistics.

Renal disease was much more likely to be listed as an associated cause of death than as the underlying cause. The use of 'multiple causes of death' coding now allows a much more complete description of the contribution to mortality of renal disease (and of other chronic diseases) than does 'single cause' coding.[3,5]

Renal disease was rarely listed alone. When renal disease was the underlying cause, there were, on average, 2.5 additional diseases or conditions. Diseases of the circulatory system were frequently recorded along with renal disease, either as an associated cause when renal disease was the underlying cause, or as the underlying cause when renal disease was an associated cause. Other diseases, such as neoplasms, respiratory disease, diabetes, and infections, were also reported in association with renal diseases, although not as frequently. These patterns are consistent with the contemporaneous occurrence of multiple chronic diseases, which accords with findings from previous studies.[6,7]

Our results suggest that almost one in four deaths with renal disease as the underlying cause would not be readily identifiable in routinely published statistics because they are due to diseases which are not included in the ICD-10 chapter on diseases of the genito-urinary system, namely hypertensive renal disease, diabetic renal disease, or congenital malformations of the kidney and ureter. No deaths were identified with diabetic renal failure as either the underlying or an associated cause. Given that diabetic nephropathy is the

second commonest cause of end-stage renal disease in Australia, accounting for 22% of new cases in 2000,[1] this suggests that the codes for diabetic renal failure (ICD-10 codes E10.23, E11.23, E13.23 and E14.23) may be under-utilised and that the relevant causes of death are instead being coded elsewhere.

The main limitation of this study is its ultimate reliance on the quality of information on death certificates, known to be imperfect.[8-10] We suggest that the listing of multiple causes of death would reduce at least one source of error, the assignment of only one disease or condition as the underlying cause.

As about 5% of deaths in Australia are not registered during the calendar year in which they occur,[11] it is likely that our analysis missed some deaths, especially those occurring in 1999. Late registration can occur when a death is referred to the coroner, when there is a delay in submitting and/or processing the form, or when a death occurs very late in the year. Although the actual numbers of people who died with renal disease as the underlying cause or as an associated cause of death are likely to be even higher than the figures presented here, it is unclear how or to what extent the proportions would be affected.

The identification of Indigenous people on death certificates is known to be incomplete and to vary across jurisdictions.[11] In addition, late registrations are about three times commoner for Indigenous deaths than for Australian deaths overall.[11] Thus the results relating to Indigenous people are an underestimate and should be interpreted with caution.

The Commonwealth, State and Territory Health Ministers have endorsed six national health priority areas: asthma, cancer control, cardiovascular health, diabetes mellitus, injury prevention and control, and mental health.[12] The focus of this national health priority initiative is disease specific. Our study has demonstrated the strong interrelationship amongst chronic illnesses, notably renal disease and cardiovascular disease and, to a lesser extent diabetes. This

interrelationship has been recognised in several recent initiatives. The National Vascular Diseases Prevention Partnership, an alliance of the Australian Kidney Foundation, the National Heart Foundation of Australia, Diabetes Australia and the National Stroke Foundation, has been established to develop common guidelines for vascular disease prevention.[13] The Northern Territory Department of Health and Community Services has developed a preventable chronic disease strategy, the first integrated non-communicable disease strategy in an Australian context. It addresses screening and intervention in an integrated program for chronic diseases, including vascular disease, early renal disease and diabetes.[14] Such initiatives are required to address what is increasingly referred to as an 'epidemic' of chronic disease of the early 21st century.

References

1. Russ GR, ed. ANZDATA Registry Report 2001. Adelaide: Australia and New Zealand Dialysis and Transplant Registry, 2002.

2. Australian Bureau of Statistics. Causes of death, Australia. Canberra: Australian Bureau of Statistics, 2000.

3. Puffer RR. New approaches for epidemiologic studies of mortality statistics. Bull Pan Am Health Organ 1989;23(4):365-83.

4. National Centre for Classification in Health. The International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM). 3rd ed. Sydney: National Centre for Classification in Health, 2002.

5. Wilkins K, Parsons GF, Gentleman JF, Forbes WF. Deaths due to dementia: An analysis of multiple-cause-of-death data. Chronic Dis Can 1999;20(1):26-35.

6. Mathur S, Gajanayake I, Hodgson G. Diabetes as a cause of death, Australia, 1997 and 1998. Canberra: Australian Institute of Health and Welfare, 2000.

7. Sarnak MJ, Levey AS. Epidemiology, diagnosis, and management of cardiac disease in chronic renal disease. J Thromb Thrombolysis 2000;10(2):169-80.

8. Nairn JR, Cobbin DM, Fett MJ, Adena MA. The quality of cause of death data for young Australian men. Aust N Z J Med 1985;15(5):609-16.

9. Weeramanthri T, Beresford B. Death certification in Western Australia--classification of major errors in certificate completion. Aust J Public Health 1992;16(4):431-4.

10. Weeramanthri TS. Reporting deaths to the coroner. Death certification needs urgent overhaul. BMJ 1993;306(6891):1539-40.

11. Cunningham J, Paradies Y. Occasional paper: Mortality of Aboriginal and Torres Strait Islander Australians. ABS cat. no. 3315.0. Canberra: Australian Bureau of Statistics, 2000.

12. de Looper M, Bhatia K. Australian health trends 2001. Canberra: Australian Institute of Health and Welfare, 2001.

13. National Public Health Partnership. Highlights of public health activity in Australia 2000-2001. Melbourne: National Public Health Partnership, 2002.

14. Weeramanthri T, Morton S, Hendy S, Connors C, Rae C, Ashbridge D. Northern Territory preventable chronic disease strategy - overview and framework. Darwin: Territory Health Services, 1999.

Table 1. Renal disease as a cause of death, Australia, 1997-99.

Type of renal disease	ICD-10 codes	Deaths with renal disease as: The underlying cause		An associated cause†	
		No.	% of all deaths	No.‡	% of all deaths
Renal failure					
Diabetic renal failure	E10.23, E11.23, E13.23, E14.23	0	0.0	0	0.0
Hypertensive renal failure	I12.0, I13.1, I13.2	1237	0.3	834	0.2
Acute renal failure	N17	916	0.2	8409	2.2
Chronic renal failure	N18	2276	0.6	8935	2.4
Unspecified renal failure	N19	1780	0.5	10672	2.8
Total renal failure		6209	1.6	26675	7.0
Other renal disease					
Diabetic renal disease	E10.2, E11.2, E13.2, E14.2 (excluding E10.23, E11.23, E13.23 and E14.23)	353	0.1	115	0.0
Hypertensive renal disease	I12.9, I13.0, I13.9, I15.0, I15.1	62	0.0	41	0.0
Other diseases of the kidney and ureter	N00-N16, N20-N29	1092	0.3	1881	0.5
Congenital malformation of the kidney and ureter	Q60-Q63	172	0.0	174	0.0
Total other renal disease		1679	0.4	2189	0.6
Total renal disease		7888	2.1	28012	7.4

†But not the underlying cause.

‡More than one associated cause may appear on a given death certificate. Causes are not mutually exclusive, so figures may add up to more than 100%.

Table 2. Characteristics of people with renal disease as the underlying cause of death, Australia, 1997-99.

	Renal failure		Other renal disease		Total renal disease	
	No. of deaths	% of all deaths	No. of deaths	% of all deaths	No. of deaths	% of all deaths
Total	6209	1.6	1679	0.4	7888	2.1
Sex						
Male	2916	1.5	756	0.4	3672	1.8
Female	3293	1.8	923	0.5	4216	2.3
Age (years)						
Less than 45	43	0.1	140	0.5	183	0.6
45-64	259	0.5	326	0.6	585	1.1
65-74	717	0.9	489	0.6	1206	1.6
75-84	2659	2.2	444	0.4	3103	2.6
85 and over	2531	2.6	280	0.3	2811	2.8
Indigenous Status						
Identified as Indigenous	113	2.1	99	1.8	212	3.9
Other	6096	1.6	1580	0.4	7676	2.1
Place of residence†						
New South Wales	2212	1.7	597	0.4	2809	2.1
Victoria	1818	1.9	388	0.4	2206	2.3
Queensland	866	1.3	344	0.5	1210	1.8
South Australia	576	1.7	117	0.3	693	2.0
Western Australia	464	1.5	132	0.4	596	1.9
Tasmania	162	1.5	40	0.4	202	1.8
Northern Territory	51	2.1	39	1.6	90	3.7
ACT	54	1.4	20	0.5	74	1.9

†Not shown are 8 deaths (6 with renal failure, 2 with other renal disease) with place of residence recorded as 'other'.

Table 3. Associated causes of death when renal disease was the underlying cause of death, Australia, 1997-99.

Cause of death (ICD-10 codes)	No. of mentions†	% of mentions†
Diseases of the circulatory system (I00-I99)	6629	33.7
Hypertensive disease (I10-I15)‡	176	0.9
Ischaemic heart disease (I20-I25)	1709	8.7
Cerebrovascular disease (I60-I69)	719	3.7
Other diseases of circulatory system (I00-I09, I26-I52, I70-I99)	4025	20.5
Diseases of the respiratory system (J00-J99)	2833	14.4
Diseases of the genito-urinary system (N00-N99)	2784	14.2
Acute renal failure (N17)	1188	6.0
Chronic renal failure (N18)	580	3.0
Unspecified renal failure (N19)	472	2.4
Other diseases of the kidney and ureter (N00-N16, N20-N29)	286	1.5
Other diseases of the genito-urinary system (N30-N99)	258	1.3
Endocrine, nutritional and metabolic diseases (E00-E90)	1241	6.3
Diabetes (E10-E14)§	583	3.0
Other endocrine, nutritional, metabolic (E00-E07, E15-E90)	658	3.3
Infectious and parasitic diseases (A00-B99)	1033	5.3
Symptoms, signs and ill-defined (R00-R99)	969	4.9
Injury, poisoning and other external causes (S00-Y98)	899	4.6
Diseases of the digestive system (K00-K93)	764	3.9
Mental and behavioural disorders (F00-F99)	663	3.4
Neoplasms (C00-D48)	465	2.4
Diseases of blood and blood-forming organs (D50-D89)	391	2.0
Diseases of nervous system & sense organs (G00-H95)	369	1.9
Diseases of musculoskeletal system & connective tissue (M00-M99)	333	1.7
Diseases of the skin and subcutaneous tissues (L00-L99)	155	0.8

Congenital malformations (Q00-Q99)¶	73	0.4
Certain conditions originating in the perinatal period (P00-P96)	45	0.2
Pregnancy and childbirth (O00-O99)	0	0.0
Total	19646	100.0

†Figures are based on the number of times particular causes appeared on death certificates, rather than on the total number of deaths. A death certificate may have more than one associated cause, and each would be reflected in the table. Therefore figures are not mutually exclusive and may add up to more than 100%.

‡Includes hypertensive renal failure and hypertensive renal disease.

§Includes diabetic renal failure and diabetic renal disease.

¶Includes congenital malformations of the kidney and ureter.

Table 4. The underlying cause of death when renal disease was listed as an associated (but not the underlying) cause of death, Australia, 1997-99.

Underlying cause of death	No. of deaths	%†
Diseases of the circulatory system	12703	45.3
Hypertensive disease‡	62	0.2
Ischaemic heart disease	7137	25.5
Cerebrovascular disease	1427	5.1
Other diseases of the circulatory system	4077	14.6
Neoplasms	5573	19.9
Endocrine, nutritional and metabolic diseases	2360	8.4
Diabetes§	1744	6.2
Other endocrine, nutritional and metabolic diseases	616	2.2
Diseases of the digestive system	1961	7.0
Diseases of the respiratory system	1734	6.2
Infectious and parasitic diseases	905	3.2
Injury, poisoning and other external causes	608	2.2
Diseases of the genito-urinary system¶	532	1.9
Diseases of the nervous system & sense organs	399	1.4
Diseases of musculoskeletal system and connective tissue	398	1.4
Mental and behavioural disorders	350	1.2
Diseases of blood and blood-forming organs	194	0.7
Diseases of the skin and subcutaneous tissues	124	0.4
Congenital malformations††	114	0.4
Perinatal conditions	50	0.2
Symptoms, signs and ill-defined	7	0.0
Pregnancy and childbirth	0	0.0
Total	28012	100.0

†Percent of deaths with a renal disease as an associated but not the underlying cause of death.

‡Excluding hypertensive renal disease and hypertensive renal failure.

§Excluding diabetic renal disease and diabetic renal failure.

¶Excluding diseases of the kidney and ureter.

††Excluding congenital malformation of the kidney and ureter.

Table 5. Relationship of renal disease with other selected causes of death, Australia, 1997-99.

Causes of death listed on the death certificate†	No. of deaths‡	% of renal deaths‡	% of al deaths
Renal disease and circulatory disease§	25528	71.1	6.7
Renal disease and ischaemic heart disease§	11990	33.4	3.2
Renal disease and cerebrovascular disease§	3787	10.6	1.0
Renal disease and respiratory disease§	11307	31.5	3.0
Renal disease and neoplasms§	7278	20.3	1.9
Renal disease and infectious & parasitic diseases§	5143	14.3	1.4
Renal disease and diabetes§	5115	14.2	1.4
Renal disease, circulatory disease and diabetes§	4098	11.4	1.1
Total renal deaths	35,900	100.0	9.5

†Includes both underlying and associated causes.

‡Combinations are not mutually exclusive, so numbers may add up to more than the total number of deaths or more than 100%.

§With or without other causes.

APPENDIX 4: Cause of Death in Patients with End Stage Renal Disease: Assessing Concordance of Death Certificates with Registry Reports.

Publication details:

Li SQ, Cass A, Cunningham J. Cause of Death in Patients with End Stage Renal Disease: Assessing Concordance of Death Certificates with Registry Reports. Submitted August 2002 *Australia and New Zealand Journal of Public Health.*

Abstract

Objectives: To assess concordance in the reporting, in two Australian national data sets, of the cause of death of patients with end-stage renal disease (ESRD).

Methods: In respect of deaths during 1997-1999, we compared 'cause of death' and 'primary renal disease', as noted in the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA), with the 'underlying' and 'associated' causes of death (based on death certificates), as recorded by the Australian Bureau of Statistics (ABS). Dates of birth and death and sex identified the same individuals in the two data sets. Cause of death was compared at the ICD-10 chapter level.

Results: Among 3,035 ANZDATA patients who died during 1997-99, 1,144 (38%) could be matched to a record in the ABS data set. Median age at death was 67, with 19% aged 75 or above. The death certificates of 237 (21%) of these 1,144 patients made no mention of non-acute renal failure. Using ANZDATA information on cause of death and ABS underlying cause of death, concordance at the ICD-10 chapter level was 38%. Using additional information on primary renal disease (ANZDATA) and/or any of up to 12 associated causes of death (ABS), concordance increased to 91%. Among all deaths in the ABS data set, 5,109 death certificates recording non-acute renal failure as the underlying cause of death did not match an ANZDATA record. For this group, median age at death was 83, with 85% aged 75 and above.

Conclusion and implications: Death certificates and ANZDATA records provide differing causes of death for ESRD patients. Information from these sources was not directly comparable. Neither data set provided a complete picture of renal disease as a cause of death.

Introduction

Data on cause of death are widely used to characterise the population burden of specific diseases. However, the information available depends on the purpose of the data collection. The Australian Bureau of Statistics (ABS) collects and reports data from death certificates as part of routine monitoring of population mortality. Deaths are currently coded using the Tenth Revision of the International Classification of Diseases.[1] Each death is assigned an 'underlying cause' and up to 12 'associated causes of death', based on information recorded in the death certificate.[2]

By contrast, the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA) collects data on mortality to address service provision for ESRD patients. Deaths are assigned to one of five broad categories which contain 42 causes of death.[3] Renal diseases are absent from this list; they are recorded as separate data on primary renal disease. Despite the differences in purpose and in coding causes of death, end-stage renal disease registry data are often compared with data from the general population.[4,5]

Perneger and colleagues in the United States discussed concordance on cause of death, for ESRD patients, between death certificates and registry reports.[6] They found that these sources provided different information on causes of death and were not interchangeable. The comparability of analogous Australian data has not previously been assessed. That is the aim of this study.

Methods

Data sets

ANZDATA maintains a data-base of patients treated in Australia by maintenance dialysis or renal transplantation.[3] The registry is funded by the Commonwealth and State governments and the Australian Kidney Foundation. All renal units providing ESRD treatment participate in the Registry. Survey forms for all patients, completed six-monthly, include cause of death. The only patients not registered are the few who die before being established on a maintenance dialysis or transplant program.[7]

The ABS death data set is based on death certificates provided by the State and Territory Registrars. Official coders at the ABS extract data from death certificates using World Health Organisation guidelines according to the ICD-10-Australian Modification (ICD-10-AM).[1]

We studied deaths that occurred in Australia during 1997 to 1999 and were registered by 31 December, 1999. We could match only those deaths for which date of birth (one of our criteria for matching) was recorded in the ABS data set. These dates were available for deaths registered in New South Wales, the Australian Capital Territory, South Australia, Western Australia and the Northern Territory. Victoria, Queensland and Tasmania only recorded age, but approximately 1% of people usually resident in these three states died in jurisdictions where date of birth is recorded. Of all deaths recorded by the ABS, 54% included date of birth.

Data matching

ANZDATA and ABS records were matched by exact dates of birth and death and by sex. With the exception of two (0.2%) ANZDATA records which matched more than one ABS record, all matches were unique one-to-one matches. We selected the matching records for these two based either on extra data about

concordance of the state of residence or extra data showing concordance of causes of death.

For all matching records, the recorded cause of death in the two data sources was compared at the level of ICD-10 chapter. ANZDATA data on cause of death and primary renal disease were re-coded to the most appropriate ICD-10 chapter (Table 1). ABS data on underlying and associated causes of death were grouped by ICD-10 chapter.

Concordance was assessed in three steps. First, the ABS underlying cause of death was compared with the ANZDATA cause of death. For example, if the death certificate recorded ischaemic heart disease as the underlying cause of death and ANZDATA recorded a cardiac or vascular disease as the cause of death, this was considered a first-level match. For those without a first level match, the comparison was repeated using all associated causes of death from the death certificate. Using the example above, if the ANZDATA cause of death was a cardiac or vascular disease and any of the associated causes of death from the death certificate included a disease of the circulatory system, then a second-level match was achieved. Finally, for those without a first- or second-level match, all underlying and associated causes of death based on death certificates were compared with the primary renal disease recorded in ANZDATA. For example, if diabetes was listed as an underlying or associated cause of death in ABS and the primary renal disease in ANZDATA was a diabetes-related code, this was considered a third-level match.

Comparison of matched records with unmatched records among deaths with non-acute renal failure as the underlying cause of death

In the ABS data set, we identified deaths where non-acute renal failure was recorded as the underlying cause. We defined non-acute renal failure to include chronic renal failure (ICD-10 code N18), hypertensive renal failure (ICD-10 codes I12.0, I13.1 or I13.2), diabetic renal failure (ICD-10 codes E10.23, E11.23, E13.23 or E14.23), and unspecified renal failure (ICD-10 code N19). We compared deaths attributed to non-acute renal failure in the ABS, but which

did not match an ANZDATA record, to all deaths for which a match was achieved. All matching and analysis was performed using Stata Release 6 (College Station, TX).

Ethical approval

We obtained ANZDATA approval to analyse de-identified data for ESRD patients who died during 1997 to 1999. We obtained approval for the project from the Joint Institutional Ethics Committee of the Royal Darwin Hospital and the Menzies School of Health Research and from the Northern Territory University Ethics Committee.

Results

Among 3,035 ANZDATA patients who died in 1997-99, 1,144 (38%) matched one of the 378,832 records in the ABS data set. ANZDATA patients were more likely to match an ABS record if they were female, non-Indigenous, or if the death occurred earlier in the period (Table 2).

Among the 1,144 matched records, the death certificates of 237 ANZDATA patients (21%) made no mention of non-acute renal failure, either as the underlying or an associated cause of death. Of these, 78 (33%) had received a transplant, but the remaining 159 (67%) were recorded as being dialysis patients at the time of death. The most commonly recorded underlying cause of death for these 237 patients was cardiovascular disease (38%), followed by neoplasms (16%) and endocrine diseases including diabetes (15%).

Among the 1,144 matched records, the ABS and ANZDATA data sets showed differing patterns of cause of death (Table 3). Although both data sets listed cardiovascular diseases as the commonest underlying cause of death, the proportion attributed to cardiovascular disease was much higher for ANZDATA (52%) than for ABS data (35%). Diseases of the genitourinary system were the second commonest underlying cause of death on ABS records (23%), but almost no deaths had been coded to this category in ANZDATA. ANZDATA records these diseases under primary renal disease rather than as a cause of death. Similarly, endocrine, nutritional and metabolic diseases, including diabetes, were the third commonest underlying cause of death (15%) in ABS records, but were not reported at all in ANZDATA. By contrast, infection was more likely to be reported as the cause of death by ANZDATA than in ABS records. One in seven deaths were coded by ANZDATA as being due to 'social' causes (Table 3). For some of these causes, such as withdrawal from treatment, there is no direct equivalent in ICD-10 (Table 1).

Using underlying cause of death as recorded on the death certificate and the ANZDATA cause of death, 38% of matched records showed concordance on cause of death at the ICD-10 chapter level (Table 4). Concordance at this level

was more likely for cardiovascular diseases (77%) and neoplasms (67%), but less likely for infectious diseases (27%). There was almost no concordance for diseases of the genitourinary system (1%) and no concordance was observed for endocrine, nutritional and metabolic diseases (including diabetes), or for congenital malformations. Relevant conditions within these categories were included in ANZDATA as primary renal diseases rather than as causes of death. Apparent concordance on cause of death was increased by utilising additional information on associated causes of death from death certificates and on primary renal disease recorded by ANZDATA (Table 4).

There were 5,109 deaths in the ABS data set with non-acute renal failure attributed as the underlying cause, but which did not match an ANZDATA record. Of this group, 43% were recorded as having chronic renal failure, 23% hypertensive renal failure and 34% unspecified renal failure. No deaths were coded as being due to diabetic renal failure, either in this group or otherwise. The median age at death for this group was 83 years, with 85% aged 75 or above. By contrast, among the 1,144 people with matching records, the median age at death was 67 years, with only 19% aged 75 or above.

Discussion

Mortality data constitute an important source of health information on which resource allocation relies. The accuracy and consistency of death certificates and other sources of mortality data have been debated.[8-10] Both ESRD registry reports and death certificates are key sources of information for planning of preventive and treatment services for renal disease. Consistent with the findings of Perneger and colleagues in Maryland, USA,[6] we have shown substantial differences between cause-of-death reports in two Australian national information systems for the same ESRD population, even at the broad ICD-10 chapter level. The discrepancies appear to arise from differences in coding practice.

The differences suggest that death certificates and registry reports have not used the same concept of 'cause of death'.[6] The ANZDATA registry focused on issues of service delivery and quality of care. Performance indicators such as 'patient refused further treatment', 'therapy ceased for any other reason', and 'haemorrhage from transplant artery' were listed as causes of death. These descriptions were not found in death certificates, which emphasised biological mechanisms of death. ANZDATA registry mortality information cannot be considered equivalent to information from death certificates or other ICD-10 based clinical studies.

The ABS data set, based on death certificates, has its limitations. In this study, the 1,144 matched records were of people with ESRD who underwent renal replacement therapy. However, 21% of this group had no mention of non-acute renal failure in their death certificates, even though the majority were recorded as receiving dialysis at the time of death. The contribution of diabetes to deaths from renal disease also appears to have been understated in the ABS data set. Diabetic nephropathy is the second commonest cause of ESRD in Australia, being responsible for 22% of new ESRD cases in 2000[3]. However, no death certificates recorded diabetic renal failure as a cause of death, which suggests that the relevant codes (E10.23, E11.23, E12.23 and E14.23) are underutilised.

This study had a number of other limitations. First, we cannot rule out the possibility of false matches. However, we believe that the matching is valid because we used exact dates of birth and death and sex to match individuals, and found only two matched records (0.2%) which were not a one-to-one match.

Second, we used death data from only those 54% of entries in the ABS data set which recorded a date of birth. It may be difficult to extrapolate our results to the entire Australian population. However, there were broadly similar patterns of cause of death between those with a date of birth and those without.

Third, deaths occurring during 1997 to 1999, but registered after 31st December 1999, were not included. Registration in a year following the calendar year of death may happen when the death occurs late in the year, or if the death is referred to the coroner, or if there are delays in submitting and/or processing the form.[11] Late registration should explain some of the progressive fall in the proportion of deaths matched. However, more than 95% of deaths are registered in the calendar year in which they occur, a proportion which does not vary markedly between jurisdictions,[11] and we therefore do not consider that late registration was likely to affect the validity of the study overall. Indigenous deaths are three times more likely to be registered late, however,[11] and this may explain the lower proportion of matching Indigenous deaths.

The ANZDATA Registry and ABS data set provide differing descriptions of mortality among ESRD patients. Because it is not ICD-10 based, Registry reporting of cause of death has limited comparability. Neither data set provides a complete picture of mortality due to chronic renal disease in Australia. The group with matched records, all of whom had received dialysis and/or a transplant, was significantly younger than the non-matching group whose death certificates attributed non-acute renal failure as the underlying cause of death; most of the latter group would not have received ESRD treatment. Some may not have had renal failure sufficiently severe to warrant dialysis or transplantation, yet it was sufficiently significant for their death to be attributed

to renal failure. This may reflect decisions by physicians not to offer dialysis to elderly people with end-stage renal disease and may, in part, explain why the incidence of *treated* end stage renal disease in Australia, 90 persons per million in 2000[3], was much lower than in the US, where it was 308 persons per million in 2000[12]. Improvement in the quality of mortality data is needed in order to develop a clearer picture of renal disease epidemiology. This in turn, would better inform policy regarding the planning of health services for chronic renal disease.

References

1. National Centre for Classification in Health. The International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM). 3rd ed. Sydney: National Centre for Classification in Health, 2002.

2. Australian Bureau of Statistics. Causes of death, Australia. Canberra: Australian Bureau of Statistics, 2000.

3. Russ GR, ed. ANZDATA Registry Report 2001. Adelaide: Australia and New Zealand Dialysis and Transplant Registry, 2002.

4. Collins AJ, Li S, Ma JZ, Herzog C. Cardiovascular disease in end-stage renal disease patients. *Am J Kidney Dis* 2001;**38**(4 Suppl 1):S26-9.

5. Brown JH, Hunt LP, Vites NP, Short CD, Gokal R, Mallick NP. Comparative mortality from cardiovascular disease in patients with chronic renal failure. *Nephrol Dial Transplant* 1994;**9**(8):1136-42.

6. Perneger TV, Klag MJ, Whelton PK. Cause of death in patients with end-stage renal disease: death certificates vs registry reports. *Am J Public Health* 1993;**83**(12):1735-8.

7. Maisonneuve P, Agodoa L, Gellert R, et al. Distribution of primary renal diseases leading to end-stage renal failure in the United States, Europe, and Australia/New Zealand: results from an international comparative study. *Am J Kidney Dis* 2000;**35**(1):157-65.

8. Penson DF, Albertsen PC, Nelson PS, Barry M, Stanford JL. Determining cause of death in prostate cancer: are death certificates valid? *J Natl Cancer Inst* 2001;**93**(23):1822-3.

9. Lahti RA, Penttila A. The validity of death certificates: routine validation of death certification and its effects on mortality statistics. *Forensic Sci Int* 2001;**115**(1-2):15-32.

10. Johansson LA, Westerling R. Comparing hospital discharge records with death certificates: Can the differences be explained? *J Epidemiol Community Health* 2002;**56**(4):301-8.

11. Cunningham J, Paradies Y. Occasional paper: Mortality of Aboriginal and Torres Strait Islander Australians. ABS cat. no. 3315.0. Canberra: Australian Bureau of Statistics, 2000.

12. U.S. Renal Data System. 2001 Annual Data Report: Atlas of End-Stage Renal Disease in the United States. Bethesda: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2001.

Table 1. ABS and ANZDATA cause of death codes.

ICD 10 chapter		ICD-10 codes	ANZDATA cause of death codes
I	Infectious and parasitic diseases	A00-B99	Immunodeficiency due to viral infection (60), non bacterial CNS infections (312-315), shunt infections (351-355), septicaemia - site unknown (371-375), liver infections (381-385), infections of other sites not specified elsewhere (391-395)
II	Neoplasms	C00-D48	Malignant disease (56)
III	Diseases of blood and blood forming organs	D50-D89	Bone marrow depression (53)
IV	Endocrine, nutritional and metabolic diseases	E00-E90	Nil
V	Mental and behavioural disorders	F00-F99	Dialysis dementia (58)
VI	Diseases of the nervous system	G00-G99	Bacterial CNS infections (311)
VII & VIII	Diseases of the eye, ear and mastoid process	H00-H95	Nil
IX	Diseases of the circulatory system	I00-I99	Cardiac (10-17), vascular (21-28)
X	Diseases of the respiratory system	J00-J99	Chronic respiratory failure (61), lung infections (321-325)

XI	Diseases of the digestive system	K00-K93	Hepatic failure (50), pancreatitis (52), perforation of abdominal viscus (57), sclerosing peritonitis (62), infections of peritoneum (361-365)
XII	Disease of the skin and subcutanous tissues	L00-L99	Wound infections (341-345)
XIII	Disease of the musculoskeletal system and connective tissue	M00-M99	Nil
XIV	Disease of the genitourinary system	N00-N99	Uraemia caused by graft failure (51), urinary tract infections (331-335)
XV	Pregnancy, childbirth and the puerperium	O00-O99	Nil
XVI	Certain conditions originating in the perinatal period	P00-P96	Nil
XVII	Congenital malformations, deformations and chromosomal abnormalities	Q00-Q99	Nil
XVIII	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	R00-R99	Cachexia (54), unknown (55), other (59)
XIX & XX	Injury, poisoning and other external causes	S00-Y98	Suicide (42), accidental death (44)
XXI	Factors influencing health status and contact with health services	Z00-Z99	Nil
Nil			Social: Patient refused further treatment (41), therapy ceased for any other reasons (43)

Table 2. Characteristics of 1,144 matched ESRD patients, 1997-99.

	No. ANZDATA deaths	No. matched	% matched
Total	3035	1144	37.7
Sex			
Male	1631	571	35.0
Female	1404	573	40.8
Indigenous Status			
Indigenous	254	84	33.1
Non- Indigenous	2781	1060	38.1
Year of Death			
1997	925	374	40.4
1998	1031	391	37.9
1999	1079	379	35.1

Table 3. Cause of death reported to ANZDATA Registry and on death certificates for 1,144 matched ESRD patients, 1997-99.

Disease category	ABS underlying cause of death		ANZDATA cause of death	
	No.	% of deaths	No.	% of dea
Circulatory system	401	35.0	593	51.8
Genito-urinary system	258	22.6	2	0.2
Endocrine, nutritional and metabolic	168	14.7	0	0.0
Neoplasms	111	9.7	91	8.0
Digestive system	47	4.1	61	5.3
Respiratory system	34	3.0	68	5.9
Infection	30	2.6	87	7.6
Congenital malformations	25	2.2	0	0.0
Musculoskeletal system and connective tissue	23	2.0	0	0.0
Injury, poisoning and other external causes	20	1.8	8	0.7
Social	0	0.0	170	14.9
Other causes	27	2.4	64	5.6
Total	1144	100.0	1144	100.0

Table 4. Degree of agreement on cause of death at the ICD-10-AM chapter level.

Level of agreement	No.	% agreed
Level 1: ABS underlying cause agreed with ANZDATA cause of death	429	37.5
Level 2: No level 1 agreement, one of the ABS associated causes agreed with ANZDATA cause of death	326	28.5
Level 3: No level 1 or 2 agreement, ABS underlying or associated cause of death agreed with ANZDATA primary renal disease	283	24.7
No agreement	106	9.3
Total	1144	100

ALLBOOK
BINDERY
91 RYEDALE ROAD
WEST RYDE 2114
PHONE: 9807 6026