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Cost-effectiveness and socioeconomic implications of prevention and management of chronic kidney disease in type 2 diabetes

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GUIDELINES

No recommendations possible based on available evidence.*

*Refer to NHMRC 'National Evidence Based Guidelines for Diagnosis, Prevention and Management of Chronic Kidney Disease in Type 2 Diabetes' (see http://www.cari.org.au) for Levels of Evidence and Evidence Grading which were undertaken in accordance with the NHMRC Hierarchy of Evidence procedure.

SUGGESTIONS FOR CLINICAL CARE

- **Based on favourable cost studies, screening for microalbuminuria and treatment with antihypertensive medications should be routinely performed for the prevention and management of kidney disease in people with type 2 diabetes.**
- **Socio-economic factors should be considered when developing programs for prevention, and management of CKD in people with type 2 diabetes.**

BACKGROUND

Cost-effectiveness

Microalbuminuria is an asymptomatic condition that affects 20–40% of people with type 2 diabetes. Of these, only about 20% are normotensive by current criteria. The rate of progression of microalbuminuria is slower in normotensive than in hypertensive people. Its significance arises from the proportion of affected people (40–80%) who subsequently develop either cardiovascular disease (CVD) or who develop proteinuria with eventual progression to renal failure.[1] ESKD causes a significant decline in quality of life, is expensive, and is associated with considerable mortality – approximately 15 per 100 patient years of Australians undergoing dialysis die annually.[2] Based on a review of clinical trials[1] a risk multiplier of 3.29 was estimated for mortality in people with type 2 diabetes, elevated blood pressure (BP) and overt nephropathy compared with those with no nephropathy. In the Australian health sector, costs for provision of ESKD health care services has been projected to increase in the order of $A50M per year and reach more than $A800M by 2010.[3] This reflects the increasing prevalence of dialysis dependent patients and costs in the order of $A40 000 to $A45 000 per person per year.[4] These ESKD cost projections exclude the costs associated with co-morbid conditions such as CVD as well as indirect or non-health sector costs associated with ESKD.[3]

Similarly, in the USA, O'Brien *et al.*[5] highlighted that the direct costs arising from ESKD were the most expensive of 15 different complications of type 2 diabetes. ESKD in the USA costs $53 659 per annum per patient. In comparison, ischaemic stroke has an event cost of $40 616 and annual cost of $9255 and a myocardial infarction has an event cost of $27 630 and an annual cost of $2185.

The cost-effectiveness of different prophylactic strategies in type 2 diabetes has not been compared. It has been estimated that the natural history of type 2 diabetes will see 17% of people developing end stage renal failure compared with 39% who will develop cardiovascular complications.[6] The latter are the dominant considerations in the elderly microalbuminuric person with type 2 diabetes and the HOPE study suggested that ACE inhibition would be justified for macrovascular protection alone in this subgroup.[7]

Treatment with angiotensin-converting enzyme inhibitor (ACEi) and angiotensin receptor blocker (ARBs) reduces the chance of progressing from microalbuminuria to overt proteinuria and the chance of progressing from overt proteinuria to ESKD.[8,9] However, the long-term effects (over 10 years of therapy) of ARB or ACEi on kidney function in type 2 diabetes are less clear. In addition, assessment of the effects of ARB or ACEi in normotensive, microalbuminuric people with type 2 diabetes need to take into account the potential cardiovascular benefits.

The review by Boersma *et al.*[10] focused on the pharmacoeconomics of ARB and ACEi treatment of people with type 2 diabetes and nephropathy. The conclusion with respect to ARBs was considered unequivocal in that the

trials show both health gains and net cost savings compared with conventional treatment therapy, largely because of the high cost of dialysis and transplantation. The outcome with respect to the use of ACEi was concluded to be less clear due to the limited head-to-head trials comparing ACEi to ARB.

It has been demonstrated that aggressive BP reduction in hypertensive, normoalbuminuric people with type 2 diabetes reduces the incidence of microalbuminuria.[11] Taken together with the progressive lowering of recommended BP thresholds for initiating treatment of elevated BP,[12] it is possible that transition rates between stages of diabetic kidney disease will be substantially lower in the future than suggested by previous studies.[13,14]

It is important to note the assumptions inherent in cost-effectiveness analyses. A major concern about cost-effectiveness analysis is the validity of extrapolating to different populations in which costs, risk of diabetic kidney disease and effects of treatment on progression to renal failure may differ from the study population.

Socio-economic implications

Socio-economic differentials in health are widely recognized with individuals of lower socioeconomic status (SES) having a higher risk for mortality and morbidity compared with those of higher SES.[15,16] These guidelines consider evidence for socioeconomic influences as they relate to outcomes relevant to the prevention and management of CKD in people with type 2 diabetes.

The increasing prevalence of type 2 diabetes has been identified as the prime cause for the increasing prevalence of ESKD in Australia.[2,17] The duration of diabetes, age, BP control and blood glucose control have been identified in the Australian population as independent risk factors for the development of albuminuria.[18] Thus the consideration of the impact of socioeconomic factors on the diagnosis, prevention and management of CKD in people with type 2 diabetes, needs to be cognisant of factors that influence the development and treatment of type 2 diabetes, or that influence the likelihood of having undiagnosed diabetes and poorly treated hypertension and blood glucose. It is reasonable to assume that socioeconomic factors that influence the diagnosis and management of type 2 diabetes will also be important factors relevant to the progression of CKD. As the evidence relating to socioeconomic influences on the, prevention, detection and diagnosis of type 2 diabetes is addressed in other type 2 diabetes guidelines, this guideline focuses on factors that relate specifically to CKD following diagnosis of type 2 diabetes.

Socio-economic status may influence the diagnosis, prevention and management of CKD in people with type 2 diabetes as a consequence of the following:[19]

- differing access to medical services,
- a differing standard of service once accessed,
- late referral to treatment and/or specialist care,
- differing compliance with interventions,
- differing outcomes of interventions, and
- difference in the prevalence of risk factors (e.g. smoking).

As discussed in the overview to these guidelines, people from disadvantaged and transitional populations are disproportionally affected by type 2 diabetes and CKD. Factors contributing to the high incidence rates of ESKD in these groups include a complex interplay between genetic susceptibility, age of onset of diabetes, glycaemic control, elevated BP, obesity, smoking, socioeconomic factors and access to health care. Within the Australian population, indigenous Australians have an excess burden of both type 2 diabetes, albuminuria and ESKD[2,20–24] and likely represent the most marginalized group within the Australian health care setting.

Explanations offered for the excess burden of kidney disease in indigenous populations can be categorized as:[19]

- primary renal disease explanations, for example greater severity and incidence of diseases causing ESKD,
- genetic explanations,
- early development explanations, and
- socio-economic disadvantage.

During 1991–2001, 47% of ESKD cases were attributed to diabetic nephropathy among indigenous Australians, compared with 21% in non-indigenous Australians. However, low kidney biopsy rates for ESKD, approximately 20% for both non-indigenous and indigenous Australians, indicate a potential for reporting bias with respect to diabetic nephropathy. Indigenous Australians have a higher rate of comorbidity than non-indigenous Australians reflecting the generally poorer health of this group. It should be noted, however, that type 2 diabetes constitutes the greatest excess comorbidity among indigenous ESKD entrants.[25,26] Socioeconomic factors that influence the health of indigenous Australians and other marginalized groups within the Australian population are likely to affect detection, prevention and management of CKD in people with type 2 diabetes. The high prevalence of type 2 diabetes causing ESKD among indigenous Australians, and the association between poor control of diabetes and risk of progression of CKD, are consistent with disadvantage being a significant determinant of progression of kidney disease in diabetes.

Cass *et al.* note that the evidence for the association between socioeconomic status and the incidence of ESKD is inconsistent.[27] A study of the association between the level of socioeconomic disadvantage for a capital city area and the incidence of ESKD showed higher ESKD rates in more disadvantaged areas.[27] A similar study of indicators of socioeconomic disadvantage among indigenous Australians (at a regional level) and the incidence of ESKD has shown a strong correlation with an overall rank of socioeconomic disadvantage. Indigenous ESKD patients are more likely to be referred to a nephrologist late in the course of their renal disease. Late referral is associated with increased mortality on ESKD treatment and is more common in disadvantaged areas. Among indigenous ESKD patients, a poor understanding of their own CKD has been linked to non-compliance and reduced active involvement in their own management.[28] Reduced engagement with care providers and services is a risk factor for poor outcomes with CKD care.

SEARCH STRATEGY

Databases searched: The search strategies were designed to reduce bias and ensure that most of the relevant data available on type 2 diabetes were included in the present review and were similar to those detailed in the Cochrane Collaboration Reviews Handbook (Higgins JPT *et al.*).[29] The electronic databases searched were Medline, EMBASE, Cochrane Library, CINAHL, HTA and DARE. The detailed search strategy, research terms and yields are provided in Appendix 3 of the complete guideline document that can be found on the CARI website (http://www.cari.org.au).

Date of searches:

Cost-effectiveness – 1 August 2008.

Socioeconomic implications – 5 January 2009.

WHAT IS THE EVIDENCE?

Cost-effectiveness

Screening people with type 2 diabetes for microalbuminuria and intensive treatment of those with elevated BP with ACEi and ARB antihypertensive agents is supported by cost-effectiveness studies.

The cost-effectiveness of intensive BP control in people with type 2 diabetes, elevated BP and normoalbuminuria, has been evaluated in the UKPDS over a mean interval of 8.8 years.[30] The intensive BP control group ($n = 758$) achieved a mean arterial pressure of 103 mmHg (144/82 mmHg) compared with 109 mmHg (154/87 mmHg) in the usual treatment group ($n = 390$). Use of resources driven by trial protocol and in standard clinical practice were compared. The main outcome measures were, firstly, cost-effectiveness ratios calculated from use of healthcare resources and, secondly, within-trial time free from diabetes-related endpoints and projected estimates of life years gained. Compared with use of resources in standard clinical practice intensive BP control was associated with an incidental cost of £1049 per extra year free from end points (costs and effects discounted at 6% per year). When the analysis was extended to life expectancy, the incremental cost per life year gained was £720, using the same discounting procedures. This UKPDS analysis represents the first evidence suggesting that tight control of BP for hypertensive people with type 2 diabetes offers a cost-effective means of reducing the risk of complication and improving health.[30]

In a further analysis of the UKPDS study, Gray performed an evaluation of the cost-effectiveness of intensive blood pressure control with atenolol ($n = 358$) *vs* captopril ($n = 758$).[31] There was no significant difference in life expectancy between groups. However, the cost per person in the captopril group was £935 greater than in the atenolol group, because of the lower drug price and fewer admissions to hospital in the atenolol group despite having higher antidiabetic drug costs. Gray's analysis suggests that in hypertensive people with type 2 diabetes and with normal AER, control of BP based on beta blockers appears superior from a cost perspective to control based on ACEi.[31] According to Kasiske *et al.*[32] and Weidmann *et al.*,[33] it is important to note that this does not apply to people with increased AER, in whom treatment with renin angiotensin system inhibitors has been shown to reduce AER to a greater clinical extent than treatment with other agents.

Howard *et al.* undertook cost-effectiveness modelling of 'opportunistic screening and best-practice management of diabetes, elevated BP and proteinuria among Australian adults'.[34] Cass *et al.* used the model outcomes as input to the companion KHA report.[3] The study modelled the health outcomes of Life Years Saved and Quality Adjusted Life Years Saved. On the basis of the model, Cass *et al.* concluded that the best available evidence supports screening and intensive management of three risk factors for CKD, namely diabetes, high BP and protein in urine.[3]

The KHA report included modelling the cost-effectiveness of screening for proteinuria and subsequent treatment with an ACEi for people with diabetes with or without elevated BP. The authors noted that there was very limited data on both screening and treatment in normotensive patients, and that model results are indicative only and suggested 'some benefit under optimistic assumptions' with results considered as being of an exploratory nature only. Howard *et al.* resolved that further trials were required in order to determine the cost-effectiveness of ACEi interventions in microalbuminuric normotensive type 2 diabetes.[34]

Palmer *et al.* completed a health economic analysis of screening (microalbuminuria and overt nephropathy) and optimal treatment of nephropathy in hypertensive type 2 diabetes within the USA health care system.[1] The inputs to the economic modelling was based on estimates derived from a review of clinical trials. The modelling indicated screening for early stage nephropathy and optimal treatment (use of 300 mg irbesartan) in addition to the patients current treatment, results in a 44% reduction in the cumulative incidence of ESKD. The incremental cost-effectiveness ratio was in the order of $US20 000 per QALY gained for screening and optimized treatment compared with no screening. A 77% probability that screening and optimized therapy would be considered cost-effective was calculated assuming a willingness to pay threshold of $US50 000. Overall the authors considered that the modelling showed that screening and optimized treatment (with an ARB) to 'represent excellent value in a US setting'.

In relation to screening and treatment with an ACEi for the early detection and treatment of kidney disease, Craig *et al.* considered that while this was a promising primary prevention strategy for the prevention of ESKD, there was inadequate trial data to support population wide adoption (i.e. all middle and older aged Australians).[4] This review was not limited to people with type 2 diabetes. Based on review of clinical trials and estimates of the performance characteristics of tests for proteinuria, it was estimated that screening of 20 000 Australians (>50 years) would lead to subsequent treatment of 100 prescribed with ACEi and prevention of 1.3 cases of ESKD over 2–3 years. A cost benefit evaluation indicated a net cost saving for the health care system assuming a one-off dipstick screening program in

men and women over 55 based on assumed prevention of 205 cases of ESKD, 100% compliance with screening and best estimates of unit costs for screening and treatment. However, the cost-effectiveness was quite sensitive to screening costs with a reversal point noted occurring at $2 per person compared with a base assumption of $0.50. Overall savings on the base assumptions were estimated at $A70 000 (2–3 years treatment costs for ESKD). Given the sensitivity of the estimates to key areas of uncertainty with respect to ESKD risk factors in the general population including, performance of screening tests and the benefits of ACEi treatment in screen-detected low risk-subjects, it remains unclear whether population wide screening for kidney disease would do 'more harm than good'. Presumably these uncertainties would be lower in the higher risk type 2 diabetes sub group favouring adoption of screening and treatment in this setting.

Cass *et al.*,[3] Craig *et al.*[4] and Palmer *et al.*[1] determined, that given microalbuminuria does not directly cause morbidity or mortality, the effectiveness of treating microalbuminuria can be assessed by comparing the cost of treatment to the savings resulting from the presumed prevention of ESKD. However, it should be emphasized that no study has followed the effects of ACEi or other intervention in normotensive, microalbuminuric people with type 2 diabetes until the development of ESKD. Nevertheless, such analysis can aid in determining which of several approaches provides the most cost-effective treatment of microalbuminuria. It should be noted that treatment of microalbuminuria is only one of several prophylactic programs that may benefit people with diabetes, and cost-benefit analysis provides a useful tool in the efficient allocation of limited health resources.

The alternatives to screening for and treating diabetic microalbuminuria with ACEi or ARBs are to wait until elevated BP (BP > 130/85) or gross proteinuria develops before instigating therapy, or to treat all people with type 2 diabetes with ACEi or ARBs regardless of their urinary protein excretion. Palmer *et al.* considered the costs and benefits for screening for albuminuria and subsequent treatment with an ARB and discussed above.[1] Golan *et al.* considered the costs and benefits associated with treatment of all people with type 2 diabetes with an ACEi have been modelled over the lifetime of a theoretical cohort of American people with diabetes aged 50 years at time of diagnosis and who were not receiving ACEi for other reasons.[35] In this model, the effectiveness of ACEi in slowing the progression of normoalbuminuria to microalbuminuria was based on only one randomized trial of 156 normotensive, middle-aged Israeli people.[14] This trial showed that ACEi therapy was associated with an absolute risk reduction of 12.5% CI: 2–23% over 6 years. The effectiveness of ACEi is slowing the progression of microalbuminuria to diabetic kidney disease was also based on one study by.[13] In 94 normotensive middle-aged Israeli people with type 2 diabetes, AER increased over 5 years from 123 to 310 mg/24 h in the placebo group, and from 143 to 150 mg/24 h in the enalapril treatment group, showing a significant reduction in the rate of change of AER ($P < 0.05$).

In the model by Golan *et al.*[35] the transition time from macroalbuminuria to ESKD was extrapolated from data on people with type 1 diabetes.[36] Potential costs factored into the model included screening for microalbuminuria and proteinuria, drug costs and expenses incurred in treating ESKD with either dialysis or transplantation. The model also considered the effects of treatment non-compliance on cost-effectiveness and adjusted outcomes for quality of life changes. Compared with waiting until overt proteinuria develops, treating microalbuminuria with ACEi was estimated to reduce overt proteinuria from 16.8 to 10.4%, ESKD from 2.1 to 1.9% and total mortality from 15.2 to 14.7% over 10-years.[35] By comparison, treating all people with type 2 diabetes with an ACEi, rather than screening for microalbuminuria, reduced microalbuminuria from 25.3 to 18.2%, overt proteinuria from 10.4 to 9.0%, ESKD from 1.4 to 1.2% and total mortality from 14.7 to 14.6% over 10-years.[35]

ACEi treatment of overt proteinuria in normotensive, people with type I diabetes reduces the progression to ESKD by about 40%.[36] The rate of progression from gross proteinuria to ESKD is similar in people with type 1 and type 2 diabetes.[37] However, it can not be assumed that ACEi will have the same effect on the prevention of ESKD in people with type 2 diabetes as shown for people with type 1 diabetes. This is because of a greater contribution of age-related intrarenal atherosclerosis and glomerulosclerosis leading to a decline in the number of functioning glomeruli.

It is important to appreciate that cost-effectiveness is critically dependent on the life expectancy of the population it is applied to. Thus, treating microalbuminuria in elderly people will be less cost-effective than treating younger people. Cost-effectiveness is also reduced if more liberal criteria are used to diagnose diabetes or if screened people are unlikely to take prescribed medications.[35]

Cost-effectiveness also depends on the cost of ACEi. Projections based upon the current cost of ACEi may underestimate cost-effectiveness considering that many of these agents will soon be off patent and presumably substantially cheaper.[35]

Cost-effectiveness studies of screening and early treatment of diabetic kidney disease were initially performed in people with type 1 diabetes.[38] Two cost-effectiveness modelling procedures were performed, assuming conservative or optimistic effects of 50% and 75%, respectively, for ACEi in slowing progression from microalbuminuria to overt kidney disease and from overt kidney disease to renal failure. The model showed that screening and treatment at the stage of microalbuminuria provided an additional 5–8 months of life expectancy, when compared with late intervention at the stage of overt diabetic kidney disease. Screening and treatment at the microalbuminuric stage in type 1 diabetes yielded a cost of $16 500 per life year saved in the conservative model, and $7900 per life year saved in the optimistic model.[38]

Similar modelling procedures have been performed in people with type 2 diabetes. The costs of screening and treating microalbuminuria with ACEi include $20/year for an annual check for microalbuminuria and $320 for treat-

ment with an ACEi. Whether this strategy increases physician/health carer time is unclear. The cost of screening for overt proteinuria is $3.[35]

It was estimated that screening and treatment with an ACEi at the microalbuminuric stage would cost $22 900 per life year saved, when compared with waiting till overt diabetic kidney disease develops.[35] This study also suggested that treating all middle-aged people with type 2 diabetes with an ACEi would cost $7500 per life year saved, when compared with delaying ACEi therapy till the microalbuminuric stage.[35] However, this 'treat all' approach has not been subjected to clinical trials and requires further cost-effectiveness evaluation. The life-time cost of ACEi treatment of microalbuminuria has been calculated as $14,940, compared with $19 520 if ACEi are only introduced after gross proteinuria develops.[35]

Data have been obtained on renal outcomes using angiotensin receptor blockade.[39] Hypertensive people with type 2 diabetes and microalbuminuria were treated over 2 years with irbesartan (150 mg/day or 300 mg/day) or placebo. The primary outcome was the time to the onset of diabetic kidney disease, defined by persistent albuminuria in overnight specimens, with an AER <200 μg/min and at least 30% higher than the base-line level. Ten of 194 people in the 300 mg/day group (5.2%) and 19 of 195 people in the 150 mg/day group (9.7%) reached the primary end-point, as compared with 30 of 201 people in the placebo group (14.9%). Cost-effective analyses have not been performed with ARB's but these results represent a 65% reduction in risk (from 14.9% to 5.2%) for the progression of microalbuminuria to macroalbuminuria with irbesartan (300 mg/day), suggesting ARB's would at least be as cost-effective as ACEi in preventing the development of CKD.

It needs to be emphasized that the above considerations apply to normotensive people with persistent microalbuminuria, who contribute approximately 20% of the total population of people with type 2 diabetes and microalbuminuria. In the larger hypertensive subgroup, antihypertensive treatment starting with an ACEi is now standard therapy.

Socio-economic implications

Socio-economic status is an independent risk factor for CKD in people with type 2 diabetes (Evidence Level III).

The prevalence and incidence of CKD is associated with socioeconomic status, whereby increasing social disadvantage is an independent risk factor for CKD in people with type 2 diabetes. The following studies provide evidence relating to the influence of socioeconomic factors on CKD in people with type 2 diabetes.

White *et al.*[40] sought to determine whether an elevated burden of CKD is found among disadvantaged groups living in the USA, Australia and Thailand. The study used the NHANES III, AusDiab I and InterASIA databases and identified a prevalence of diabetes of 10.6% in the USA, 7.4% in Australia and 9.8% in Thailand in people 35 years or older. Crude analysis showed income in the lowest quartile, shorter duration of education and being unemployed ($P < 0.01$) to significantly increase the odds of having an eGFR <60 mL/min per 1.73 m^2. Multivariate analysis adjusting for age and gender showed no significant association in the AusDiab data. Disadvantage appeared to affect CKD prevalence in the USA via mechanisms independent of the clustering of risk factors in groups by SES. The association between disadvantage and CKD did not appear to be internationally consistent.

A cohort of 650 patients living within the boundary of Greater London who first attended a diabetes clinic between 1982 and 1985 was assessed by Weng *et al.*[41] Postcodes were used to determine whether the diabetes care outcomes were linked to material deprivation and place of residence. Deprivation was determined using an 'under-privileged area' UPA score based on eight variables. Proteinuria was defined as a single positive dip stick test on a morning urine sample. The mean HbA1c from deprived areas was higher than that of prosperous wards, insulin treatment was used less commonly and glycaemic control was worse. The age-adjusted prevalence of proteinuria was significantly higher ($P < 0.001$) in deprived areas being 57%, 25.6% and 21.7% in deprived, intermediate and prosperous areas, respectively. There was no significant difference in glycaemic control between ethnic groups. While more Afro-Caribbean's live in deprived areas, a higher proportion of patients from these areas were Caucasian. Obesity, poor glycaemic control and smoking habits were identified as major risk factors in relation to socioeconomic status and increased complications arising from diabetes.

Bello *et al.*[16] studied the association between area-level SES and the severity of established CKD, at presentation to a renal service in the UK. The study was a retrospective cross-sectional review of 1657 CKD patients, where CKD was defined by an eGFR of <60 mL/min per 1.73 m^2 for at least 6 months duration. A residential area deprivation index was used as an indicator of SES. The study identified an increasing trend in the severity of CKD (based on eGFR) at presentation to a renal unit in association with an increase in the area-level measure of deprivation. The most deprived areas also had the highest age-adjusted prevalence rate for CKD. Diabetes and hypertension explained a large part of the relationship between deprivation and severity of CKD. BMI, smoking, serum cholesterol, age and race did not fully explain the relationship.

A retrospective population study of the incidence and prognosis of CKD in the UK, which included a regional based assessment of socioeconomic deprivation, was undertaken by,[42] The incidence of CKD was based on a serum creatinine value of ≥1.7 mg/dL (≥150 μmol/L) with cases identified from a review of a database of chemical pathology results. The least and most deprived quintiles had rates of 1067 per million population (pmp) per annum (95% CI: 913–1221) and 1552 pmp per annum (95% CI: 1350–1754). The nature of the study did not allow for adjustment for potential confounding factors such as BMI, smoking and hypertension. Furthermore the cause of CKD was not able to be estimated for the majority (87%) of the cases.

A population based prospective study aimed at identifying how much of the excess risk for CKD among African Americans can be explained on the basis of racial disparities in potentially modifiable risk factors was conducted by.[43] The following explanations of the higher incidence of ESKD among African Americans were considered:

- SES,
- Greater prevalence and severity of diabetes and hypertension, and
- Increased inherited susceptibility to kidney damage.

The study analysed baseline CKD risk factors from a non-concurrent nationally representative population based cohort (NHANES II) with a 12–16 year follow-up. Compared with white subjects, African American adults were more likely to have lower educational attainment, live below the federal poverty line and to be unmarried. They were also more likely to be current smokers, to be obese, to be physically inactive and to drink less alcohol. They had a higher prevalence of diabetes and hypertension as well as higher SBP and GFR. The age-adjusted incidences of all-cause CKD and treated ESKD were 2.7 and 8.9 fold higher among African Americans. The age-adjusted incidence of kidney disease attributable to diabetes was almost 12 times higher in African Americans. After adjustment for age and gender, sociodemographic factors, lifestyle factors and clinical factors, the excess risk of CKD among African Americans reduced from a relative risk of 2.69 (1.50–4.82) to 1.95 (1.05–3.63); explaining 44% of the excess risk. Diabetes and hypertension alone accounted for 32% of the excess risk. The differences according to ethnicity were greater with middle aged than older adults. The authors concluded that interventions aimed at reducing racial disparity in CKD risk should focus on primary prevention and improved treatment of diabetes and hypertension, lifestyle modification, and elimination of health disparities attributable to socioeconomic status.

The Fremantle Diabetes Study reported by Davis *et al.*,[44] a longitudinal observational study in a community based clinically-defined type 2 diabetes patient cohort, compared the ACR in self-identified Aboriginal and Torres Strait Islanders ($n = 18$) with Anglo Celt type 2 diabetes patients ($n = 819$), who represent the largest ethnic group within the patient community. The Aboriginal and Torres Strait Islander patients were significantly younger at diagnosis but had similar diabetes duration. Despite similar glycaemic management, the indigenous patients had higher HbA1c. The geometric mean ACR was significantly higher in Aboriginal compared with Anglo Celt patients (10.1 (1.1–93.6) vs. 2.9 (0.7–12.4) mg/mmol, respectively). The SBP and DBP were lower and the smoking rate three times higher than in the Anglo Celt patients. Even though Aboriginal and Torres Strait Islander patients had a higher number of GP visits each year, they were less likely to have received diabetes education or to self monitor blood glucose. Overall there was no significant difference in the proportion of each group that died during the mean follow up period of 9.3 ± 3.2 years, however, the age at death was 18 years younger in the Aboriginal group. Aboriginal patients had a twofold higher risk of dying than Anglo Celts. Among other variables, urinary ACR was an independent predictor of all-cause mortality in Aboriginal and Torres Strait Islander and Anglo Celt patients. The Fremantle Study, although the small number of indigenous patients reduces the ability to draw inferences about the urban indigenous population, suggests that sustained high-level glycaemia and smoking are likely determinants of albuminuria in the Indigenous patients.

Socio-economic status is associated with reduced access to primary medical care services and a lower level of utilization of those services and this is likely to be associated with poorer outcomes in relation to CKD in people with type 2 diabetes (Evidence Level IV).

The mechanisms by which social disadvantage increases the risk of CKD have not been fully elucidated. However, social disadvantage appears to influence the stage of CKD at which specialist referral takes place, which in turn has negative implications for individual outcomes. Access to and utilization of primary care medical services may also be lowest among those of highest social disadvantage and greatest need, thereby limiting the ability for implementation of interventions shown to prevent or reduce progression of CKD.

Consideration of access to medical services needs to take into account both services related to prevention as well as specialist care for the management of CKD. Consistent with the study by Davis *et al.*,[44] the socially disadvantaged are likely to be less educated in aspects of primary prevention and management. In relation to CKD, the timing of referral to a nephrologist might further influence the progression of CKD and overall outcomes. The meta analysis by Chan *et al.*[45] examined the outcomes in patients with CKD referred late to a nephrologists. The analysis did not distinguish between the cause of CKD nor conduct sub group analyses for diabetes. Overall, 20 studies (total sample size 12 749) examined the effect of late referral met inclusion. The definition of late referral varied from 1 month to 6 months. There was a significantly increased overall mortality in the late referral group compared with the early referral group (relative risk 1.99 95% CI: 1.6–2.39) and a significantly longer duration of hospital stay. However, the mean serum creatinine and creatinine clearance at time of referral were not significantly different between the groups.

Cass *et al.*,[46] investigated the association between area level measures of socioeconomic disadvantage and the proportion of ESKD patients who were referred late for renal replacement therapy. The analysis, which utilized the ANZDATA database, considered the timing of referral to a nephrologists and the postcode of residence at the start of treatment. Late referral was defined as those who required dialysis within 3 months of referral. The analysis was restricted to capital cities and excluded overseas visitors and those where ESKD was caused by disease with very short course. The ABS Statistical Sub-Division (SSD) level socioeconomic data from the 1996 census was used for the assessment.

Of the total of 3334 patients (April 1995 – December 1998), 889 (26.7%) were found to have been referred late with a high variability between SSDs. There was a significant correlation between late referral and disadvantage

($r = 0.36$, $P = 0.01$), with a higher proportion of late referral being associated with the more disadvantaged regions. Areas with higher incidence of ESKD in population terms were also areas where a higher proportion of patients were referred late. Issues of access, availability and quality of care are all potentially relevant to late referral. Disadvantaged areas had both an increased population burden of ESKD and a greater risk of delayed access to specialist renal services which is then associated with a poorer outcome. The study concludes that despite an overall improvement in the prevention and care of chronic diseases, with regard to chronic renal failure, there is a failure to address the needs of general practitioners and the public especially in disadvantaged areas. Of interest, late referral was found not to be related to geographical access to dialysis units.[46]

Overland *et al.* analysed information on the number of diabetic individuals and number of services for selected Medicare item codes by NSW postcodes using the Health Insurance Commission data file.[47] The analysis was conducted for the 1996 calendar year and indicated that people at most disadvantage were less likely to be under the care of a GP (OR 0.41 0.40–0.41) or consultant physician (0.50 0.48–0.53) despite this group having the highest prevalence of diabetes. Once under care, slightly more were likely to undergo HbA1c or microalbuminuria screening (1.04 1.00–1.10 and 1.22 1.12–1.33) but less likely to undergo lipid or HDL cholesterol (0.81 0.48–0.53 and 0.85 0.79–0.90). Thus while disadvantaged people had poor access, once in the health system the level of monitoring received was similar. They note, however, that the majority of medical practitioners are located in capital cities yet the majority of people in NSW at most social disadvantage live outside the Sydney metropolitan area. In addition the gap between Medicare reimbursement and the amount charged by medical practitioners is often greater in rural areas. People at most social disadvantage may be selectively disadvantaged in regard to access to health care services in the current system. The reluctance to test the most socially disadvantaged group for lipid abnormalities may reflect the cost of lipid lowering treatment (at the time of the survey).

The relationship between social disadvantage and access to GPs is further demonstrated in the study by Turrell *et al.*[48] who conducted an analysis of 1996–1997 Medicare data to evaluate associations between utilization of GPs, socioeconomic disadvantage, geographic remoteness and Indigenous status. The review was undertaken at the level of Statistical Local Areas (SLA) after assigning an Index of Relative Socio-economic Disadvantage (IRSD) and Accessibility/Remoteness Index of Australia (ARIA). The proportion of Indigenous Australians was calculated from the number of self-identified persons of Aboriginal and Torres Strait Islanders background. In relation to socioeconomic disadvantage the following points were noted:

- the number of full time equivalent GPs decreased with decreasing socioeconomic status and increasing remoteness of SLAs,
- the proportion of Indigenous Australians increased with decreasing socioeconomic status and increasing remoteness of SLAs,
- the utilization rate of GP services decreased markedly with the remoteness of the SLA and to a lesser extent with decreasing socioeconomic status, and
- there was an interaction between remoteness and socioeconomic disadvantage such that:
  - in highly accessible areas average GP utilization rate increased with decreasing SES, and
  - in remote/very remote areas, the average GP utilization rate decreased with decreasing SES.

The authors concluded that in areas of adequate GP supply, ready geographic and financial access, equity of access appears to prevail. However, in socioeconomically disadvantaged areas where GPs are least accessible and affordable, the principle of equity of access to services is compromised. Furthermore, these latter areas are also those with highest medical needs.

SUMMARY OF THE EVIDENCE

- The best available evidence supports screening and intensive management of the three risk factors for CVD, namely diabetes, high blood pressure and protein in urine.
- Screening for albuminuria in people with type 2 diabetes has been modelled as being cost-effective due to the anticipated reduction in CVD events and the reduction in the number progressing to ESKD. The modelling shows cost-effective outcomes both with respect to life years saved as well as quality adjusted life years saved.
- Similarly treatment of albuminuria with ACEi and ARB antihypertensive agents is a cost-effective approach to reducing CVD outcomes and progression to ESKD.
- The cost-effectiveness of treating normotensive microalbuminuric type 2 diabetes patents with an ACEi and/or ARB antihypertensive agent has yet to be established.
- Further studies on the benefits of ACE inhibition in preventing ESKD in normotensive microalbuminuric people with type 2 diabetes would allow better estimates of the cost-effectiveness of this treatment. However it may be difficult to ethically justify such studies
- The prevalence and incidence of CKD is associated with socioeconomic status, whereby increasing social disadvantage is an independent risk factor for CKD in people with type 2 diabetes.
- The mechanisms by which social disadvantage increases the risk of CKD have not been fully elucidated. However, social disadvantage influences access and utilization of medical services, thereby limiting the ability for implementation of interventions shown to prevent or reduce progression of CKD.

WHAT DO THE OTHER GUIDELINES SAY?

KDOQI: Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease, AJKD, Suppl 2. 49(2):S46, February 2007.

No recommendation.

UK Renal Association: No recommendation.

Canadian Society of Nephrology: No recommendation.

European Best Practice Guidelines: No recommendation.
NICE Guidelines: National Collaborating Centre for Chronic Conditions. Type 2 diabetes: national clinical guideline for management in primary and secondary care (update). London: Royal College of Physicians, 2008.

No recommendation.

IMPLEMENTATION AND AUDIT

No recommendation.

SUGGESTIONS FOR FUTURE RESEARCH

No recommendation.

CONFLICT OF INTEREST

None identified.

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