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# Reduction in natural death and renal failure from a systematic screening and treatment program in an Australian Aboriginal community

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**Reduction in natural death and renal failure from a systematic screening and treatment program in an Australian Aboriginal community.**

*Background.* Australian Aborigines in remote areas are experiencing an epidemic of renal and cardiovascular disease. In November 1995, we introduced a renal and cardiovascular treatment program into the Tiwi community, which has a three- to fivefold increase in death rates and a recent annual incidence of treated end-stage renal disease (ESRD) of 2760 per million. Our previous study described an estimated 50% reduction in renal failure and all-cause natural deaths in the treatment group through December 31, 1998. We now describe a reduction in these events through mid 2000.

*Methods.* People eligible for treatment were those with confirmed hypertension, diabetics with microalbuminuria or overt albuminuria, and people with overt albuminuria, regardless of blood pressure and diabetes. Treatment centered around the use of perindopril (Coversyl, Servier), with additional agents as needed to reach defined blood pressure goals, attempts at control of glucose and lipid levels, and health education. Two hundred and sixty-seven people, or 30% of the adult population, have been enrolled, with mean follow up of 3.39 years. Rates of terminal endpoints were compared on an intention-to-treat basis with those of 327 historical controls matched for baseline disease severity, who were followed for a mean of 3.18 years in the pre-treatment program era, against a background of no treatment or inconsistent changing treatment.

*Results.* Terminal events occurred in 38 controls and 23 people in the treatment group. The estimated rate of natural deaths in the treatment group was 50% that of the controls, ($P = 0.012$); the rate of renal deaths was 47% ($P = 0.038$) and the rate of non-renal deaths was 54% that of controls ($P = 0.085$). Survival benefit in the treatment group was observed at all levels of overt albuminuria, in non-diabetics and diabetics, in normotensive as well as hypertensive people, and in people who had been taking angiotensin converting enzyme-inhibitors (ACEi) in the pre-program era, as well as those who had not. Benefit was absent among the low death rates of people without overt albuminuria, and questionable among people with glomerular filtration rates (GFRs) <60 mL/min. The number of people needed to treat (NNT) to avoid one terminal event of natural causes was calculated at only 11.6.

*Conclusions.* Falling rates of deaths and renal failure in the whole community support marked benefit of the program. Millions of dollars have been saved, based on avoidance of dialysis alone, but the reduction in premature death is the greater benefit. Chronic disease programs like this are enormously effective, and should be introduced into to all high-risk communities as a matter of urgency.

**Key words:** kidney disease, Tiwi and disease, community renal program, diabetes, hypertension, cardiovascular disease, albuminuria:creatinine ratio, end-stage renal disease.



Aborigines living in remote Australia have high rates of all-cause mortality, of cardiovascular deaths and of end-stage renal failure (ESRD) [1, 2], with the incidence of treated ESRD exceeding 1000 per million in some regions. Costs of treating ESRD are spiraling out of control. From 1996 to 1998, the annualized treatment costs for an Aboriginal person on hemodialysis in the Top End of the Northern Territory (NT) were estimated at $112,169:$71,000 for dialysis treatments alone and $41,169 for intercurrent hospitalizations [3]. These funds could be spent otherwise on prevention and primary care in this seriously under-resourced environment. However, premature death in young and middle aged adults is the greater tragedy.

These problems have been especially serious in the Tiwi Islands (population about 1800, about 50% age 20+ years), with high rates of premature adult death, and an incidence of treated ESRD reaching 2760 per million in the mid 1990s [2]. In the 1990s, 25% of natural deaths in Tiwi adults were renal deaths, 42% had a primary or underlying cardiovascular cause, and 43% were of neither renal nor cardiovascular cause [4].

In a community-wide screening program starting in 1990, we found cardiovascular risk factors, including type 2 diabetes and hypertension, in abundance [5]. We also found that renal disease, marked by pathologic albuminuria, was pervasive. Albuminuria progressed with age, so that fully 55% of adults were affected, and was inversely correlated with glomerular filtration rate (GFR) [6]. A

longitudinal study showed that albuminuria marked all the future risk for renal deaths, and it also strongly predicted non-renal deaths, both cardiovascular and non-renal non-cardiovascular. Overall, pathologic albuminuria marked 75% of the risk for all-case natural death over the observation period [4].

Use of antihypertensive drugs, including angiotensin converting enzyme inhibitors (ACEi), was gradually increasing in the Tiwi community through the early 1990s, but systematic management of the burden of disease exposed by our studies seemed beyond the capabilities of the health services in place. Therefore, in November 1995 we introduced a formal program to alter renal and cardiovascular disease outcomes.

We previously described the results of this program up through December 1998, when the maximum time on treatment was 3.1 years, average time on treatment was 2.1 years, and total follow up was 549 person-years [7]. The results were dramatic: blood pressures fell markedly and progression of albuminuria and decline in GFR were arrested on a group basis. When compared with historical controls who were followed for a total of 543 years in the pre-program era, the treatment group showed an estimated 50% fall in rates of all-cause natural deaths and renal failure.

We now describe the survival of the treatment cohort through June 30, 2000. Extended time on treatment has allowed a comparison with an expanded group of controls, followed for a longer period, beginning with baseline studies done earlier in the 1990s.

## METHODS

The albumin creatinine ratio (ACR, g/mol) on a random urine specimen was used as an indicator of renal disease and its severity [5, 6]. The following categories were employed: <3.4, normal; 3.4 to 33, microalbuminuria, and 34+, overt albuminuria. Overt albuminuria was further categorized thus: 34 to 99, moderate; 100 to 199 heavy; 200+ intense. Serum creatinine levels were measured, and GFR was estimated by the Cockcroft and Gault formula [8].

People eligible for treatment were those with confirmed hypertension (≥140/90 on two occasions), all diabetics with confirmed pathologic albuminuria (ACR 3.4 g/mol and above), and all persons with confirmed overt albuminuria, (ACR 34+), regardless of blood pressure or diabetes. Exclusions were people who were pregnant, breast feeding or known to be allergic to ACEi.

Medical treatment centered around the use of the long-acting angiotensin-converting enzyme inhibitor, perindopril (Coversyl, Servier), and attempts to keep blood pressures below 130/85 in the first two years of the program, and below 125/70 in the last two years [9]. The intended minimum perindopril dose was 4 mg, but the dose was increased to 8 mg for people above the blood pressure goal, and later in the program, for people of substantial body size, or with resistant overt albuminuria (ACR 60 g/mol and more). After the first year we used full-dose perinopril in people with serious renal insufficiency, finding little justification for use of smaller doses [10]. Calcium channel blockers were added if needed for blood pressure control, and diuretics were added for further blood pressure control or fluid retention. Other elements of the program included health education, and attempts to control blood glucose levels and lipids, when needed.

Enrollment into the treatment program was prioritized to some extent by disease severity. This included prioritized enrolment of several people with serious renal insufficiency who were deteriorating on their current management. Participants were followed until they died, started dialysis, or through June 30, 2000, 4.56 years after the first person was enrolled on the program. People dying an unnatural death before the end of the observation period were censored from the cohort at the time of that event. Due to irresolution in the first few months of the program, the treatment group for the final analysis included only people prescribed treatment for at least a month.

After an initial training period, the program was run by local health workers and community liaison workers. They used community lists and recall systems, relied heavily on algorithms for testing and treatment, and were required to become familiar with only a limited number of medicines. They were supported, mostly remotely, by a nurse coordinator and a doctor authorizing treatment. The program was modeled around collaborative, rather than authoritative lines, and often operated outside the clinic.

It was not ethical to have an untreated control group, nor feasible to have one treated with different regimens; thus the outcomes of the treatment group were compared with those of historical controls matched for disease severity, to the extent possible. These controls were people screened and followed in the pre-treatment-program era, who were selected, blind to their ultimate outcome, based on the following criteria on their baseline screening:

(*1*) BP ≥140/90 and diabetes or pathologic albuminuria (3.4+).
(*2*) Diabetics with pathologic albuminuria (ACR 3.4+).
(*3*) Overt albuminuria (ACR 34+) regardless of blood pressure or diabetes.

People with a single observation of elevated blood pressure, but without other risk factors, were not included as controls.

The course of controls was followed against a background of no treatment or changing treatment, from their baseline examination until they died, started dial-

**Table 1.** Characteristics of control and treatment groups

| | Controls, $N = 327$ | Intention to treat, $N = 267$ | $P$ value |
|---|---|---|---|
| Age | 21–76, 41.7 (12.8) | 21–77, 43.4 (11.4) | 0.09 |
| Female | 176/327, 53.8% | 155/267, 53.0% | 0.30 |
| BMI | 14.0–43.5, 25.8 (5.2) | 14.9–44.1, 27.0 (5.8) | 0.011 |
| SBP *mm Hg* | 76–220, 134.2 (21.4) | 88–210, 134 (20.8) | 0.93 |
| DBP *mm Hg* | 45–130, 82.4 (14.8) | 45–120, 81.2 (13.8) | 0.318 |
| Hypertension[a] | 177/327, 54.1% | 146/267, 54.7% | 0.893 |
| Diabetic | 102/327, 31.1% | 117/267, 43.8% | 0.002 |
| ACR *g/mol* | 0.7–664, 33.1 (33–44)[b] | 0.7–864, 45.1 (38–54)[b] | 0.068 |
| ACR <34 | 120/327, 36.7% | 96/265, 36.2% | 0.171[c] |
| ACR 34–99 | 132/327, 40.3% | 89/265, 33.6% | |
| ACR 100–199 | 47/327, 14.4% | 47/265, 17.7% | |
| ACR 200+ | 28/327, 8.7% | 33/265, 12.5% | |
| Creatinine *umol/L* | 33–596, 84.9 (82–88)[b] | 44–380, 87.2 (84–90)[b] | 0.33 |
| GFR *mL/min* | 9–212, 96.8 (35.2) | 18–213, 95.7 (37.4) | 0.70 |
| GFR <30 *mL/min* | 54/323, 16.7% | 38/265, 14.3% | 0.43 |

Data are range, mean (SD), or $N$ (%).
[a] Hypertension: BP ≥140/90, or on ACEi treatment prior
[b] Geometric mean (95% CI)
[c] $P$ value for difference in distribution of category of ACR

ysis, were established for at least a month in the treatment program, or until June 30, 2000. Survivors were censored 4.56 years after their qualifying observation, the maximum follow-up period of people in the treatment program. People who died unnatural deaths before 4.56 years of follow-up were right-censored at time of death.

The fate of all persons was ascertained, and a cause of death allocated by review of clinic and hospital records and death certificates. Deaths were categorized as all-cause natural death (non-renal and renal deaths), renal deaths (dialysis or death with chronic renal failure), non-renal deaths, cardiovascular deaths (primary or contributing), and non-renal, non-cardiovascular deaths. These are described in more detail elsewhere [4]. For renal deaths and for the combined end point of natural death and renal failure, the survival interval of people starting dialysis ended when treatment began.

For the treatment cohort, data were analyzed on an "intention to treat" basis. Terminal events were expressed as rates per 100 person-years. Hazard ratios for terminal events were calculated by the Cox proportional hazard method after demonstration that the assumptions of the proportional hazard model were not violated. Survival statistics also were compared by Kaplan Meier methods. STATA statistical software was used for data analysis [11].

## RESULTS

Two hundred and sixty-seven people were enrolled in the treatment program, or about 30% of all adults (20+ years). Baseline urine ACR levels and serum creatinine levels were available in 265 of these people. They were followed for a total of 898 years, with a mean (SD) of 3.36 (SD 1.16) years. Fifty-six people were no longer in the treatment program on June 30, 2000; 23 people had died or developed renal failure, one died a suicide death, six became normotensive, two were "false starts", six became pregnant, one was breast feeding, six had adverse effects (3 with cough, 2 with angioedema, 1 with itching), six decided to quit, three moved, and two went onto palliative care.

Three hundred and twenty-seven people were identified as controls. They were followed for a total of 1041 years, with a mean of 3.18 (1.48) years. One hundred and seventy-one (52.3%) were ultimately enrolled in the treatment program. The other 156 were not, for reasons that included interim death or renal failure, declining treatment, failure to confirm eligibility criteria, presence of exclusion criteria, or moving from the area.

The profiles of the treatment and control groups are compared in Table 1. The treatment group tended to be older than the controls, was more often diabetic, and tended to have higher ACR levels. Sixty-one of the treatment group, or 22.8%, had been prescribed enalapril or captopril prior to enrollment.

Medical treatment intensified over time. Of people participating at three years, 2% were prescribed 2 mg perindopril, 32% were prescribed 4 mg perindopril and 66% were prescribed 8 mg perindopril. Seventeen percent of people (all on maximum perindopril) were taking a single additional medicine (calcium channel blockers or diuretics) and 5.7% were taking both agents. By self-report in the middle and later parts of the program, 66% of people were taking their medicines "most of the time," 27% "sometimes" or "occasionally", and 7% "rarely or never" [12].

Over the course of treatment, there was a rapid, marked, and sustained drop in blood pressure, and a retardation of both the progression of albuminuria and the loss of

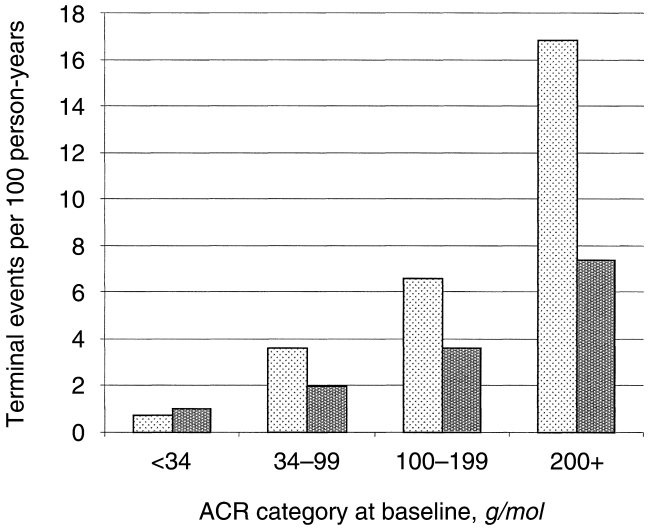


**Fig. 1. Rates of all-cause natural death, by baseline albuminuria:creatinine ratio (ACR) category for controls (□) versus treatment cohort (■).**

GFR on a group basis. These observations are described separately [7, 12–14].

Sixty-one people reached a terminal event of natural cause: 38 in the control group, and 23 in the treatment group. Twenty-five (41%) of these were renal deaths, of whom 21 went onto dialysis. Thirty-six deaths (59%) were non-renal. Twenty-nine deaths (45.9%) had a primary or underlying cardiovascular cause.

Figure 1 summarizes the treatment program effect. It shows that rates of all-cause natural deaths were strongly related to baseline ACR category, and that rates were lower in the treatment group than in controls for persons in every category of overt albuminuria. No difference was apparent among the low death rates of people with lower ACRs.

Table 2 shows the numbers and rates of terminal events by baseline ACR in the control and treatment groups. It shows lower rates of all-cause natural death for the treatment groups in all categories of overt albuminuria, illustrated in Figure 1. It also shows the numbers and rates by category of death, with people with ACR 100+ consolidated into a single group, due to smaller numbers of type-specific events. All renal deaths but one were segregated among people with baseline ACR 100+ (the other with a baseline ACR of 99.5), and the rate in the treatment group was apparently lower than in controls. Rates of non-renal deaths, cardiovascular deaths and non-renal non-cardiovascular deaths were lower also for the treatment group than for controls in aggregate, and for people in both categories of overt albuminuria.

Table 3 summarizes the hazard ratios of the treatment group relative to controls, for each category of endpoint, adjusted for age, sex and baseline ACR level. It shows a 50% reduction in rates of all-cause natural deaths in the treatment group, and a 57% reduction in renal deaths, both of which are significant. It also shows a 46% reduction in non-renal deaths, a 49% reduction in deaths with a cardiovascular component, and a 61% reduction in non-renal, non-cardiovascular deaths, although these associations escaped significance.

Table 4 shows the estimated reduction in all-cause natural death in the treatment group according to participant characteristics and baseline renal function, with adjustment for age and sex and ACR. Although the smaller numbers reduce the significance of the associations, there was a suggestion of treatment benefit in people with elevated blood pressures as well as those with lower blood pressures, in non-diabetics as well as diabetics, and in people who had previously been on ACEi treatment as well as those who had not. The data confirm lack of benefit in people without overt albuminuria. Among people with ACRs 34+ there was a 57% reduction in rates of natural death, which was significant.

Survival benefit of treatment took about two years to become manifest as shown in Figure 2.

Figure 3 shows that the numbers of natural deaths and of the people starting dialysis in the entire community began to fall at about the time of enrollment of substantial numbers of people in the treatment program. Aggregate data from other Aboriginal communities across the Top End of the NT, where screening and treatment policies are changing more slowly, have not reflected the same sharp changes.

## DISCUSSION

The introduction of a systematic screening and treatment program into this high risk community was associated with an estimated 50% reduction in rate of natural deaths and 57% reduction in rate of renal failure at an average follow up of 3.39 years, when compared with the fate of people with similar disease severity in the pre-treatment program era.

Heightened awareness, health education, and better metabolic management were all elements of the program, but most of the treatment benefit was probably due to medication for renal and cardiovascular protection. The fall in blood pressures, the reduced progression of ACR, and reduction in the loss of GFR, predict reductions in renal and all-cause natural deaths, as we have observed.

There are many problems with the methods used to estimate treatment benefit in this program. One serious source of understatement of treatment benefit was the intentional recruitment into the treatment group of several people with progressive renal insufficiency who were failing their status quo management. This reduced the real rates of renal failure in the natural history and exacerbated rates of renal failure early in the treatment pro-

**Table 2.** Terminal events in controls versus treatment group

| Natural endpoints by category | ACR category | Controls *events/person-year* | Controls *events/100 person-year* (95% CI) | Treatment *events/person-year* | Treatment *events/100 person-year* (95% CI) |
|---|---|---|---|---|---|
| All cause | All | 38/1041.2 | 3.64 (2.66–5.05) | 23/897.8 | 2.56 (1.73–3.92) |
| | <34 | 3/422.4 | 0.71 (0.23–2.20) | 3/310.6 | 1.00 (0.31–3.0) |
| | 34–99 | 15/417.1 | 3.60 (2.17–5.96) | 6/307.7 | 1.95 (0.88–4.27) |
| | 100–199 | 9/136.5 | 6.59 (3.43–12.6) | 6/167.5 | 3.58 (1.61–7.98) |
| | 200+ | 11/65.2 | 16.8 (9.34–30.5) | 8/108.5 | 7.38 (3.69–14.7) |
| Renal | All | 14/1041.1 | 1.34 (0.8–2.27) | 11/897.8 | 1.23 (0.68–2.21) |
| | <34 | 0/422.4 | 0 | 0/310.5 | 0 |
| | 34–99 | 1/417.1 | 0.24 (0.03–1.70) | 0/307.7 | 0 |
| | 100+ | 13/201.7 | 6.44 (3.74–11.1) | 11/275.9 | 4.0 (2.21–7.2) |
| Nonrenal | All | 24/1041.2 | 2.31 (1.55–3.43) | 12/897.8 | 1.34 (0.76–2.35) |
| | <34 | 3/422.4 | 0.71 (0.23–2.20) | 3/310.5 | 0.97 (0.31–3.0) |
| | 34–99 | 14/417.1 | 3.36 (2.0–5.67) | 6/307.2 | 1.96 (0.88–4.34) |
| | 100+ | 7/201.7 | 3.47 (1.65–7.28) | 3/275.9 | 1.09 (0.35–3.37) |
| Cardiovascular | All | 18/1041.23 | 1.73 (1.09–2.74) | 10/897.8 | 1.11 (0.6–2.07) |
| | <34 | 0/422.4 | 0 | 1/310 | 0.32 (0.05–2.28) |
| | 34–99 | 9/417.1 | 2.16 (1.12–4.15) | 3/307.7 | 0.98 (0.31–3.02) |
| | 100+ | 7/201.7 | 3.47 (1.65–7.28) | 3/275.9 | 1.09 (0.34–3.37) |
| Non-renal, non-cardiovascular | All | 13/1041.2 | 1.25 (0.72–2.15) | 5/897.8 | 0.56 (0.23–1.34) |
| | <34 | 0/422.4 | 0 | 1/310.5 | 0.32 (0.04–2.29) |
| | 34–99 | 9/417.1 | 2.16 (1.12–4.15) | 3/307.7 | 0.98 (0.31–3.02) |
| | 100+ | 4/201.7 | 1.98 (0.74–5.28) | 1/275.9 | 0.36 (0.05–2.57) |

**Table 3.** Hazard ratios by category of endpoint; treatment vs. controls adjusted for age, sex and baseline ACR

| | HR (95% CI), treatment vs. controls |
|---|---|
| All-cause natural death | 0.50 (0.36–0.86), $P = 0.012$ |
| Renal | 0.43 (0.19–0.96), $P = 0.038$ |
| Non-renal | 0.54 (0.21–1.09), $P = 0.085$ |
| Cardiovascular | 0.51 (0.23–1.13), $P = 0.097$ |
| Non-renal, non-cardiovascular | 0.39 (0.14–1.14), $P = 0.085$ |

gram. The use of historical controls to estimate treatment benefit is also imperfect. First, the courses of the groups were not precisely contemporaneous. Second, the controls were followed over a background of no treatment and changing treatment, which could not be precisely delineated. Third, eligibility of controls by ACR levels was assessed on a single examination, whereas confirmation was required for the treatment group while people with a single elevated blood pressure, but no other eligibility criteria, were excluded as controls. Fourth, more than half the control group subsequently entered the treatment program, and having avoided death and renal failure in the pre-program era, thus might have defined themselves as "survivors," potentially inflating the treatment program benefit. However, the greater age, more diabetes, and more severe renal disease in the treatment group, all survival disadvantages, could contribute to understatement of the program's benefit. Ultimately, trends in community-based deaths and renal failure supported the marked impact of the program, although the community included people who qualified for, but did not receive treatment (because they were not screened, could not access treatment, or did not want it).

Despite a good outcome, the results of such a program could be better. The "intention to treat" analysis understates the full potential treatment benefit, because ≥34% of people were taking medicines occasionally, or not at all. Hypertension, and therefore eligibility for treatment even in the absence of albuminuria, should be redefined as BP ≥130/80 in this high risk population [10]. Blood pressure control was not optimum; at two years 44% of the treatment group had BPs >125/70, a desirable level for people with renal disease [9]. Control of blood glucose and lipid levels needs to improve. According to the HOPE study, application of ACEi treatment in diabetics can be expanded [15]. Finally, wider use of other renal-protective drugs such as angiotensin receptor blocking agents, and possibly higher doses of ACEi in poor responders, should be applied [16].

Treatment appeared to be of benefit in people with normal blood pressures at baseline and those with hypertension, in non-diabetics as well as diabetics, and in people who had previously received ACEi treatment, as well as those who had not. Benefit was apparent among people with all categories of overt albuminuria, who comprised 64% of the treatment group, although not among the very low death rates of people with lower levels of urinary albumin. Finally, treatment appeared to be more effective in avoiding end points in people with better preserved GFRs. However, the clear improvement in blood pressure in people with low ACRs

**Table 4.** Numbers of all-cause natural death by patient characteristics and renal function, and hazard ratio, controls vs. treatment, adjusted for age, sex, and ACR

| Group | Controls | Treatment | Adjusted Hazard Ratio (95% CI) *Treatment vs. Controls* |
|---|---|---|---|
| | *Events/person-year* | | |
| BP <140/90 | 17/433.3 | 14/503.1 | 0.55 (0.26–1.14), $P = 0.106$ |
| BP ≥140/90 | 21/598 | 9/395 | 0.48 (0.20–0.99), $P = 0.050$ |
| Non-diabetics | 26/735.1 | 10/510.2 | 0.47 (0.22–1.02), $P = 0.055$ |
| Diabetics | 13/302.6 | 14/400.4 | 0.52 (0.24–1.13), $P = 0.098$ |
| Treatment group, no prior ACEi | 38/1041.2 | 18/662.2 | 0.60 (0.34–1.06), $P = 0.079$ |
| Treatment group, prior ACEi only | 38/1041.2 | 5/235.6 | 0.32 (0.14–0.84), $P = 0.020$ |
| ACR <34 | 3/422.4 | 3/310.5 | 1.26 (0.24–6.57), $P = 0.784$ |
| ACR 34+ | 35/618.8 | 20/587.4 | 0.43 (0.25–0.76), $P = 0.004$ |
| GFR <60 | 22/160.5 | 14/108.5 | 0.78 (0.39–1.56), $P = 0.475$ |
| GFR 60+ | 16/880.7 | 9/789.4 | 0.44 (0.19–1.09), $P = 0.059$ |

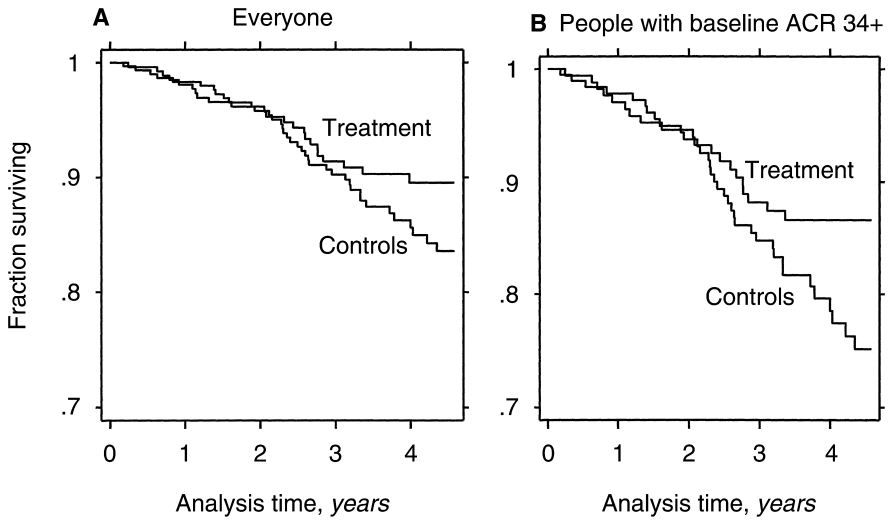


**Fig. 2. Unadjusted Kaplan-Meier estimated survival rates for everyone (*A*) and those with a baseline ACR of 34+ (*B*) in the treatment versus control groups.**

and low GFRs people [7, 12, 13, 14] suggest that survival benefit will become manifest in these groups over a longer period of follow-up period.

Survival benefit was reflected in reduced renal and nonrenal deaths. Reduction in renal deaths has important implications for morbidity, mortality and costs, while the 54% reduction in nonrenal deaths has a tremendous impact in terms of premature death avoided or postponed.

Our demonstration that albuminuria predicts nonrenal as well as renal deaths [4], anticipates a reduction in natural deaths and renal failure through interventions that retard the progression of albuminuria. A fall in cardiovascular deaths is expected in view of the antihypertensive and cardiac and vascular-sparing effects of ACEi. However, the associations of non-cardiovascular non-renal deaths with albuminuria and the apparent benefit with treatment lend themselves less readily to traditional explanations.

About two years of treatment was required before reduction in all-cause natural death became apparent. This reflects, in part, the prioritization of the sickest people for early entry into the program. It also implies that the reductions in blood pressure, progression of ACR and loss of GFR that occur with treatment take time to translate into measurable survival benefits.

Our data suggest that a terminal end point was avoided in about 23 people in the treatment cohort: approximately 13 renal deaths and 10 non-renal deaths. Thus, the number of people needed to treat (NNT) over an average of 3.39 years to avoid a terminal end point was only 11.6, and the NNT to avoid one renal death was 26.7. Thus, the program was both effective and efficient in avoiding unwanted outcomes. It also saved costs. Baker et al estimated the average annual cost per patient in the treatment cohort over the first three years of the program was $1,383 [17]; this would fall as people move from the start-up to the maintenance phase. Using dialysis cost estimates of You et al [3] and the average survival of people on dialysis described by Spencer et al [2], it was estimated that between $884,400 and $4,057,200 was saved in those first three years, through avoidance or postponement of dialysis alone. The range depends on whether ESRD incidence would have plateaued at the pre-program peak of 2760 per million (pm), or would have continued to double every four years in the absence

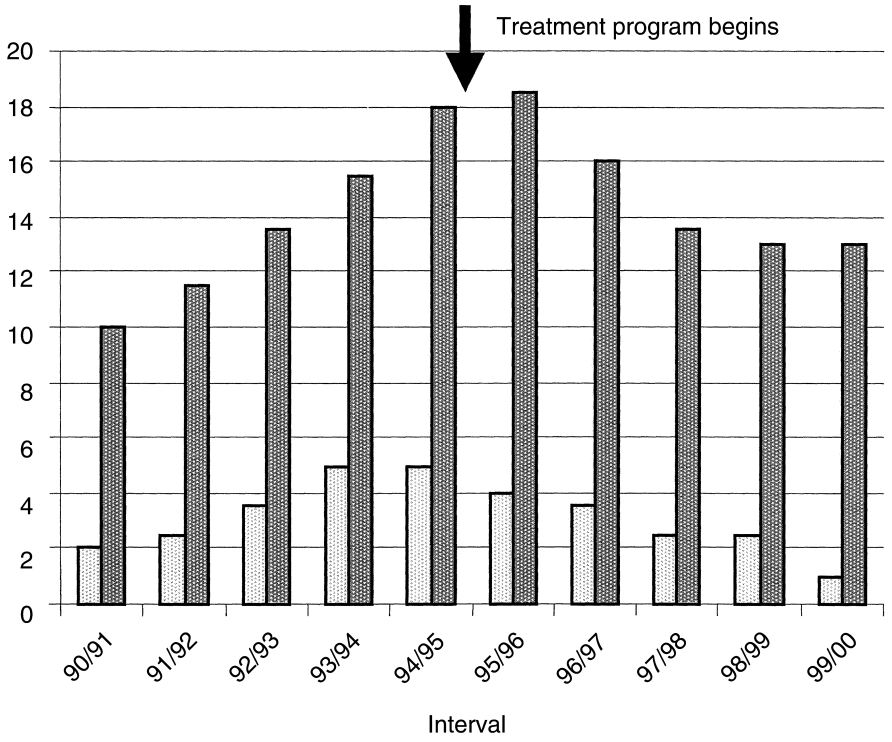


**Fig. 3. Average annual number of natural deaths (□) and new dialysis starts (■) in Tiwi adults.**

of intervention [17, 18]. The analysis through mid-2000 suggests that the program continues to save costs on the basis of dialysis avoided. If we included savings through reduced hospitalizations and through allocation of a monetary value to years of life gained in young and middle aged adults, the savings would be even more impressive.

Much of this program's success derives from a strong sense of community ownership and control, a non-judgmental, non-authoritarian style, and respect for competing personal and community perspectives and priorities. Individuals appreciate personalization of their health goals, and many are slowly adopting lifestyle changes [19].

Most Aboriginal health services in remote Australia are under-resourced. Deficiencies in the prevention, surveillance and management of chronic diseases are especially notorious, despite the morbidity, mortality and costs these conditions are generating. This project has shown that Aboriginal people are interested in health issues, receptive to health messages, and willing to take medicine over the long term against a future health risk, with an excellent clinical response. It also shows that, in the specific instance of renal disease, considerable costs are saved by a systematic approach to regular testing and treatment. These principles, which merely represent good practice, should be incorporated into regular adult health care in all Aboriginal communities as a matter of urgency [20] and resourced appropriately. Similar programs, varying in details according to local realities, could also bring much benefit to high-risk populations in developing countries [21].

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The participants in this program gave informed consent to have their course followed in the context of the projects "The epidemiology and prevention of Aboriginal renal disease, Parts 1 and 2." These were approved by the Joint Institutional Ethics Committee of the Menzies School of Health Research and Territory Health Services, and its Aboriginal subcommittee, and by the Tiwi Land Council (Part 1), and by the Tiwi Health Board (Part 2).

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## REFERENCES

1. Cunningham J, Condon J: Premature mortality in Aboriginal adults in the Northern Territory. *Med J Aust* 165:309–312, 1996
2. Spencer JS, Silva D, Hoy WE: An epidemic of renal failure among Australian Aborigines. *Med J Aust* 168:537–541, 1998
3. You J, Hoy WE, Beaver, Eagar K: Costs of treating people with end stage renal disease in the Northern Territory. *Med J Aust* 176:461–465, 2002
4. Hoy WE, Wang Z, Baker PRA, *et al*: The natural history of renal disease in Australian Aborigines, Part 2. The predictive value of albuminuria for premature death and renal failure. *Kidney Int* 60:249–256, 2001

5. Hoy WE, Pugsley DJ, Normal RJ, Hayhurst BG: A brief heath profile of adults in a Northern Territory Aboriginal community: With an emphasis on preventable morbidities. *Aust N Z J Public Health* 21:121–126, 1997
6. Hoy WE, Mathews JD, Pugsley DJ, *et al*: The multidimensional nature of renal disease: Rates and associations of albuminuria in an Australian Aboriginal community. *Kidney Int* 54:1296–1304, 1998
7. Hoy WE, Baker P, Kelly A, Wang Z: Reducing premature death and renal failure in Australian Aborigines: Results of a community-based treatment program. *Med J Aust* 172:473–478, 2000
8. Cockcroft D, Gault MK: Prediction of creatinine clearance from serum creatinine. *Nephron* 16:31–41, 1976
9. The Sixth Report of the Joint National Committee on Prevention: Detection, Evaluation and Treatment of High Blood Pressure (JNC VI). *Arch Intern Med* 157:2413–2446, 1997
10. Ruggenenti P, Perna A, Remuzzi G: ACE inhibitors to prevent end stage renal disease: when to start and why possibly never to stop: A post hoc analysis of the REIN trial results. *J Am Soc Nephrol* 12:2832–2837, 2001
11. Statacorp: *Stata Statistical Software* (Release 6.0). College Station, TX, Stata Corporation, 1999
12. Hoy WE, Baker P, Kelly A, *et al*: Stemming the tide: Reducing cardio-vascular disease and renal failure in Australian Aborigines. *Aust N Z J Med* 29:480–483, 1999
13. Hoy WE, Wang Z, Baker PRA, *et al*: Secondary prevention of renal and cardiovascular disease: results of a renal and cardiovascular treatment program in an Australian aboriginal community. *J Am Soc Nephrol* 14 Suppl: (in press), 2003
14. Hoy WE, Wang Z, Baker PRA, *et al*: The natural history of renal disease in Australian Aborigines, Part 1. Progression of albuminuria and loss of glomerular filtration rate over time. *Kidney Int* 60:243–248, 2001
15. The Heart Outcomes Prevention Evaluation Study Investigators: Effects of an angiotensin converting enzyme inhibitor, Ramipril, on death from cardiovascular causes, myocardial infarction and stroke in high-risk patients. *N Engl J Med* 342:145–153, 2000
16. Mackenzie HS, Ziai F, Omer SA, *et al*: Angiotensin receptor blockers in chronic renal disease: The promise of a bright future. *J Am Soc Nephrol* 10(Suppl 12):S283–S286, 1999
17. Baker PRA, Hoy WE, Wang Z, Glaziou P: Preventing renal failure in Australian Aborigines: An effectiveness and cost analysis of a screening and treatment program. Presented at the 35th Annual Scientific meeting of the Australian New Zealand Society of Nephrology, 3–5 March, 1999
18. Baker PRA: *Cost-effectiveness analysis of a treatment program to prevent end stage renal disease in an Australian Aboriginal community.* PhD Thesis submitted through the University of Queensland, Australia, and the Menzies School of Health Research, Northern Territory, Australia, 2000
19. Kelly A, Tipiloura E, Hoy WE, *et al*: Compliance with a renal disease prevention program in an Australian Aboriginal community. Presented at the 35th Annual Scientific meeting of the Australian New Zealand Society of Nephrology, 3–5 March, 1999
20. Hoy WE: Screening and treatment for renal disease: The community model. *Nephrology* 4(Suppl iii–iv):S90–S95, 1998
21. Hoy WE: Reflections on the 15th International Congress of Nephrology. Renal and cardio-vascular protection in the developing world. *Nephrol Dial Transplant* 16:1509–1511, 2001