Supplemental Materials and Methods

The eGFR Baseline and Follow-up Studies were approved by the joint Menzies School of Health Research – Northern Territory Department of Health Human Research Ethics Committee, including the Aboriginal sub-committee. The study was also approved by the Central Australian Human Research Ethics Committee, Human Research Ethics Committee Cairns and Hinterland, Royal Perth Hospital Ethics Committee and Western Australian Aboriginal Health Information and Ethics Committee.

Measurements performed in The eGFR Baseline Study included non-fasting blood samples [creatinine, c-reactive protein (CRP), HbA1c], reference GFR (4 hour plasma disappearance of iohexol), urine ACR, blood pressure, anthropometry (weight, height, waist, hips), medical history, and socio-economic questionnaire. These measurements were commenced in November 2007 (pilot data collection in 2007/08), and the majority of baseline data were collected in 2009-2010.

Participants and recruitment

Potential participants (Figure 1) for the clinical assessment were contacted by a research team member by telephone where feasible, or through participating Aboriginal Medical Services or health clinics (by word-of-mouth or clinic staff members contacting the participant). Local community members were employed to facilitate contact of participants.

As outlined in Figure 1, 619 participants were eligible for follow-up in the eGFR follow-up study. Eight (1.3%) participants could not be located by the time of this analysis and are therefore considered lost to follow-up. A further 14 (2.3%) participants were excluded because they had a follow-up time of less than six months and one (0.2%) participant was

excluded after being found ineligible for participation because of acute deterioration of kidney function due to intercurrent illness at baseline.

Examination Protocol for the Clinical Assessment:

The follow-up assessment was done on one occasion between 2 to 4 years after the baseline assessment. The assessment protocol was:

1. Renal Function: creatinine and eGFR (assessed by CKD-EPI formula) were analysed at a central laboratory where possible (see below). Iohexol GFR was not performed at follow-up.

2. Medical history and medications were recorded.

Data collection techniques for follow-up from medical records

If a participant was unavailable or un-contactable, the following were established through medical records (primary care, hospital and pathology companies) with consent from baseline assessment: vital status, progression to renal replacement therapy (RRT), blood test results for creatinine, HbA1c and urine ACR. If no information was available through medical records, then vital status was confirmed with primary health clinic staff. Of the 619 participants initially eligible for follow-up, 15 were excluded and 8 were unable to be located (Figure 1). Of the remaining 596 participants followed up, 400 were seen at the follow-up visit and 196 were followed through medical records (after baseline measurement, 46 of whom had no follow serum creatinine measurement recorded). Thus a total of 550 participants had a follow-up serum creatinine result and are included in the current analysis. Of the 400 participants seen at the follow-up visit, 396 participants had a serum creatinine performed at the central laboratory at both baseline and follow-up. The reasons the 196 participants were not seen at a follow-up visit were: away at the time the team visited for follow-up (n=31); moved away from the study location (n=83); not interested in participating

in follow-up (n=32); unknown to the community or unable to be found (n=34); or died before the end of the follow-up period (31/1/2014, n=16). No date of death was recorded for 1 participant but their death was within the follow-up study period. Category of cause of death (renal or non-renal) was determined from medical records and Northern Territory Coroner's Office where applicable.

Laboratory methods

Blood samples were collected into lithium heparin and serum separating tubes and centrifuged for 10 min at 3000 revolutions per min within 4 hours of collection. If unable to be centrifuged immediately, blood was stored in a cool environment (fridge or cooler with freezer blocks) until centrifugation. Following centrifugation, serum and plasma specimens were transported on ice to be stored at -80 degrees Celsius (-80 ^{0}C). For blood samples collected in remote locations, after processing, storage for transportation was either on dry ice or in liquid nitrogen ("Biological Shipper", CryoPak Series, Taylor-Wharton, AL, USA). Samples collected in several remote locations, including Thursday Island, Queensland were stored at -30 ^{0}C after processing, for 2-14 days prior to transportation on dry ice to a -80 ^{0}C freezer.

The same creatinine method was used at baseline and follow-up for enzymatic creatinine measured at Melbourne Pathology, Melbourne, Australia (Cobas c701, Roche Diagnostics, Mannheim, inter-assay CV of 2.1% at 79 umol/L and 1.3% at 519 umol/L). Serum creatinine and other biochemical tests were also performed at each centre as part of standard clinical care. We ensured that the creatinine assay at each centre were traceable to the IDMS reference method (1). To ensure comparability across centres, all stored specimens were measured for enzymatic creatinine at Melbourne Pathology.

A total of 46 (7.7%) participants had no follow-up serum creatinine assessment, and one of these died. Methods used for creatinine assays of 550 participants in the current analysis were: enzymatic creatinine (Melbourne Pathology) at baseline and follow-up for n=369 participants; local laboratory standard clinical care creatinine at baseline and follow-up for 121 participants (where the same local laboratory was used at both baseline and follow-up); enzymatic creatinine (Melbourne Pathology) at baseline and local laboratory at follow-up for n=53 participants; and local laboratory standard clinical care creatinine at baseline and follow-up for n=7 participants (where a different local laboratory was used at baseline and follow-up but nil enzymatic creatinine available at baseline). Among the total of 181 participants with local pathology measurement of serum creatinine at baseline and follow-up, 19 participants (3.2%) initiated RRT and 13 (2.2%) died during the follow-up period

Urine ACR was measured by local pathology providers using several methods(2), with previous reports confirming adequate agreement between laboratories using these methods(3). Urine ACR results for 7 participants were excluded due to growth on culture consistent with urine tract infection (specimens were sent for microscopy and culture if urinalysis results were positive for leucocytes or nitrites).

Data handling and statistical methods

At the time of assessment, data were collected on paper forms and subsequently entered into The eGFR Follow-up Study Microsoft Access database. Further details regarding Statistical analyses outlined in the manuscript included below. Backwards selection was used for the multivariable model of eGFR change to eliminate non-informative variables with a p-value of 0.1 or more. Data were analysed in aggregate and according to strata of kidney function.

Baseline clinical characteristics of the 596 participants followed-up (with follow-up blood analyses (n=550) and without follow-up blood analyses (n= 46) were compared using medians (inter-quartile ranges) for continuous variables and frequencies (proportions) for categorical variables. For participants with follow-up blood analyses, the baseline clinical characteristics were stratified by baseline eGFR categories (<60 ml/min/1.73m^2,60-90 ml/min/1.73m^2 and ≥90 ml/min/1.73m^2). A difference between participants with and without a follow-up blood sample was assessed using ANOVA for continuous variables and Chi-Square test for categorical variables. A significant difference in the annual change of eGFR according to baseline eGFR and ACR categories was assessed using general linear models with the baseline eGFR of ≥90 ml/min/1.73m^2 and ACR <3.0mg/mmol as a reference category. Cox proportional hazards models were used to assess relationships with the dichotomous combined renal end-point. The assumption of proportional hazards was assessed visually using Schoenfeld residuals. To avoid any violations to the proportional hazards assumption, Cox proportional hazards models were stratified by baseline eGFR levels <60 mls/min/1.73m2, 60-90 mls/min/1.73m2 and >90 mls/min/1.73m2.

References

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