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Incident CKD Over 5-Years in a Population-Based Study of Apparently Healthy Young Adults at Risk of Mesoamerican Nephropathy (MeN)

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Introduction:
Mesoamerican Nephropathy (MeN) has led to the death of tens of thousands of young adults across rural Central America. We recently reported eGFR decline of over 30mL/min/1.7m² over 2 years among substantial numbers of apparently healthy young adults from rural communities in northwest Nicaragua. The consequences of this early loss of eGFR is not known.

Methods:
The original 350 participants (a rural, population-based sample, aged 18-30 years, male:female ratio 3:1, without reported diabetes, hypertension or CKD) from the study have been followed-up annually for a further 3 years (visits 6-8). An additional 417 men and women (ratio 1:1) recruited using the same criteria in October 2018, have also now been followed up for 1 year (visits 7 and 8). Serum creatinine was measured in two batches (visits 1-5 and visits 6-8) in the UK at laboratories using IDMS reference standards. Historic samples were retested to capture batch effects and results from the second batch normalised to the first. eGFR was then calculated by CKD-EPI formula. Baseline CKD was defined as an eGFR<60mL/min/1.7m² on the first two visits and de novo CKD was defined as those participants from the original cohort without baseline CKD who developed an eGFR <60mL/min/1.7m² on at least two serial measurements without recovery.

Results:
Mean bias between the two batches of creatinine tests was minimal (-0.6micromol/L; 95%CI -1.5 to 0.3). Across all participants at baseline (mean age 23.3 years) 87% of men and 98% of women had an eGFR≥90mL/min/1.7m², but despite excluding those self-reporting kidney disease, 3% of males had CKD at this time. In the original cohort, 90% participants attended ≥5 of the 8 study visits. eGFR varied substantially visit-to-visit such that 38% of men and 6% of women had an eGFR<90mL/min/1.7m² at some point during the 5- year follow-up. Furthermore, among men (but not women), 9% had an eGFR<60mL/min/1.7m² (at ≥1 visit),
4.2% developed de novo CKD and 0.8% (n=2) died from kidney failure over the follow-up. The distribution of eGFR for males and females over the 8 visits (60 months) is shown in the Figure.

Discussion:
Within person eGFR fluctuates substantially in this population at high-risk of MeN. This likely reflects important biological effects making longitudinal studies critical for disease insight. Nonetheless over time there is both a substantial loss of eGFR across the population and unprecedented rates of incident CKD among young men. When compared to the reported prevalence of CKD stages 3-5 of 0.1% amongst men of a similar age-range in England, the calculated incidence of de novo CKD in males of ~1% per year in our study, underlines the scale of the problem. There is an urgent need to understand the aetiology of MeN so preventative measures can be instituted.