Identification of young adults at risk of accelerated kidney function loss in an area affected by Mesoamerican nephropathy

Marvin Gonzalez-Quiroz[1,2,3], Evangelia-Theano Smpokou[3], Neil Pearce[2], Ben Caplin[3]*, Dorothea Nitsch[2]*

[1]Research Centre on Health, Work and Environment (CISTA), National Autonomous University of Nicaragua at León (UNAN-León), León, Nicaragua. [2]Department of Non-Communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK. [3]Centre for Nephrology, University College London, London, UK.

Supplementary Material

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Figure S1: Bland-Altman for eGFR based on serum creatinine levels measured in Nicaragua and serum creatinine levels measured in London.

A. Agreement between eGFRscr-Oxford and eGFRscr-Nicaragua at baseline
The dashed lines on the Bland-Altman graphs indicate mean and grey area the limits of agreement (-37.24 to 16.30 mL/min/1.73m2).

B. Agreement between eGFRscr-Oxford and eGFRscr-Nicaragua at second study visit
The dashed lines on the Bland-Altman graphs indicate mean and grey area the limits of agreement (-35.09 to 18.30 mL/min/1.73m2).

C. Agreement between eGFRscr-Oxford and eGFRscr-Nicaragua at third study visit
The dashed lines on the Bland-Altman graphs indicate mean and grey area the limits of agreement (-26.29 to 33.17 mL/min/1.73m2).
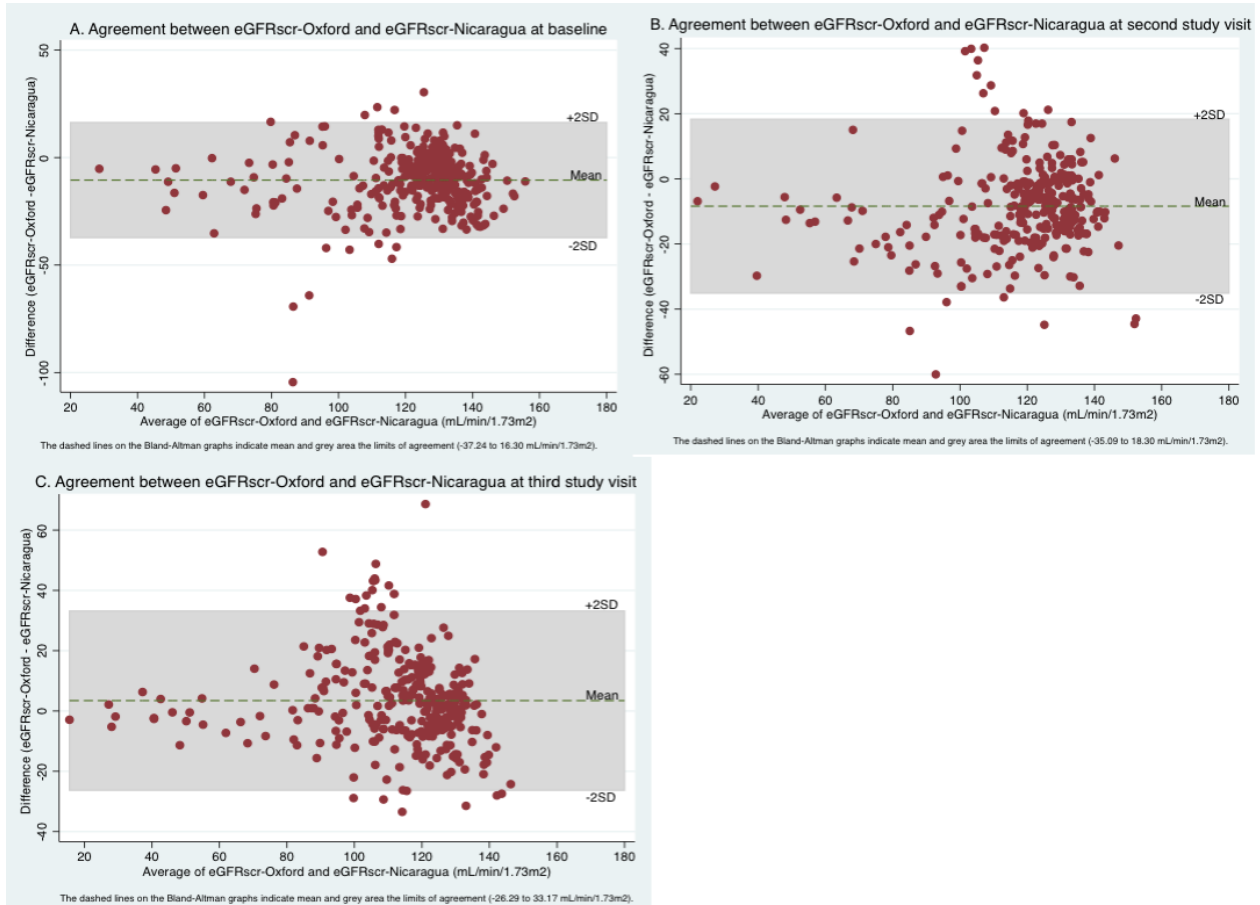
Table S1: Multivariate adjusted logistic regression analysis for eGFR and uNGAL associated with established renal dysfunction at baseline among apparently healthy young males

Factors	Model 1 (n=80)				Model 2 (n=80)			
	Without uNGAL levels				With uNGAL levels			
	Coefficient	SE	95% CI	P-value	Coefficient	SE	95% CI	P-value
$eGFR_{Scr}$ at baseline	-0.14	0.03	-0.22 to -0.07	<0.001	-0.15	0.04	-0.24 to -0.06	<0.001
Urinary NGAL	--	--	--	--	3.16	1.44	0.34 to 5.99	0.028

Abbreviations: SE: standard error, uNGAL: urinary neutrophil gelatinase-associated lipocalin, $eGFR_{Scr}$: estimated glomerular filtration rate based on locally measured creatinine levels.

Table S2: Multivariate adjusted logistic regression analysis for eGFR and uNGAL associated with a rapid decline in kidney function at baseline among apparently healthy young males

Factors	Figure 2A								Figure 2B			
	Model 3 without uNGAL levels (n=79)				Model 4 with uNGAL levels (n=79)				Model 5 without uNGAL levels (n=68)			
	Coefficient	SE	95% CI	P-value	Coefficient	SE	95% CI	P-value	Coefficient	SE	95% CI	P-value
$eGFR_{Scr}$ at baseline	0.003	0.01	-0.02 to 0.03	0.808	0.004	0.01	-0.02 to 0.03	0.798	-0.01	0.01	-0.04 to 0.02	0.507
Urinary NGAL	-	-	-	-	0.81	0.45	-0.06 to 1.70	0.070	-	-	-	-
$eGFR_{Scr}$ at second study visit	-	-	-	-	-	-	-	-	-0.06	0.02	-0.10 to -0.01	0.015
$eGFR_{Scr}$ at third study visit	-	-	-	-	-	-	-	-	-	-	-	-

Abbreviations: SE: standard error, uNGAL: urinary neutrophil gelatinase-associated lipocalin, $eGFR_{Scr}$: estimated glomerular filtration rate based on locally measured creatinine levels.

Continued: Table S2: Multivariate adjusted logistic regression analysis for eGFR and uNGAL associated with a rapid decline in kidney function at baseline among apparently healthy young males

Factors	Figure 2B				Figure 2C							
	Model 6 with uNGAL levels (n=68)				Model 7 without uNGAL levels (n=73)				Model 8 with uNGAL levels (n=73)			
	Coefficient	SE	95% CI	P-value	Coefficient	SE	95% CI	P-value	Coefficient	SE	95% CI	P-value
$eGFR_{Scr}$ at baseline	-0.01	0.01	-0.04 to 0.02	0.501	0.01	0.01	-0.01 to 0.05	0.328	0.01	0.01	-0.01 to 0.05	0.330
Urinary NGAL	0.54	0.95	-0.57 to 1.65	0.310	-	-	-	-	0.56	0.56	-0.54 to 1.67	0.319
$eGFR_{Scr}$ at second study visit	-0.05	0.02	-0.10 to -0.006	0.025	-	-	-	-	-	-	-	-
$eGFR_{Scr}$ at third study visit	-	-	-	-	-0.06	0.01	-0.09 to -0.02	<0.001	-0.05	0.01	-0.09 to -0.02	0.001

Abbreviations: SE: standard error, uNGAL: urinary neutrophil gelatinase-associated lipocalin, $eGFR_{Scr}$: estimated glomerular filtration rate based on locally measured creatinine levels.

Continued: Table S2: Multivariate adjusted logistic regression analysis for eGFR and uNGAL associated with a rapid decline in kidney function at baseline among apparently healthy young males

Factors	Figure 2D							
	Model 9 without uNGAL levels (n=67)				Model 10 with uNGAL levels (n=67)			
	Coefficient	SE	95% CI	P-value	Coefficient	SE	95% CI	P-value
eGFR$_{Scr}$ at baseline	-0.004	0.01	-0.04 to 0.03	0.812	-0.004	0.01	-0.04 to 0.03	0.798
eGFR$_{Scr}$ at second study visit	-0.02	0.02	-0.07 to 0.02	0.404	-0.01	0.02	-0.06 to 0.03	0.485
eGFR$_{Scr}$ at third study visit	-0.06	0.02	-0.10 to -0.02	0.002	-0.06	0.02	-0.10 to -0.02	0.002
Urinary NGAL	-	-	-	-	0.44	0.66	-0.86 to 1.74	0.508

Abbreviations: SE: standard error, uNGAL: urinary neutrophil gelatinase-associated lipocalin, eGFR$_{Scr}$: estimated glomerular filtration rate based on locally measured creatinine levels.

Table S3: Multivariate adjusted logistic regression analysis of factors associated with established renal dysfunction at baseline among apparently healthy young males

| Factors | Model 1 (n=74) | | | | Model 2 (n=74) | | | |
| | Without uNGAL levels | | | | With uNGAL levels | | | |
	Coefficient	SE	95% CI	P-value	Coefficient	SE	95% CI	P-value
Age	0.14	0.22	-0.29 to 0.57	0.525	0.12	0.22	-0.30 to 0.56	0.563
Season								
Summer	0.0	--	--	--	0	--	--	--
Winter	1.00							
Outdoor work								
Yes	7.14	4.14	-0.97 to 15.26	0.084	7.57	5.42	-3.05 to 18.20	0.162
No	1.00				1.00			
Urinary ACR								
≥30 mg/g	0	--	--	--	0	--	--	--
<30 mg/g	1.00				1.00			
Urinary NGAL	--	--	--	--	3.31	1.87	0.35 to 6.99	0.077
eGFR$_{Scr}$ at baseline	-0.26	0.10	-0.47 to -0.05	0.014	-0.27	0.13	-0.54 to -0.005	0.045

Abbreviations: SE: standard error, uNGAL: urinary neutrophil gelatinase-associated lipocalin, UACR: urinary albumin creatinine ratio, eGFR$_{Scr}$: estimated glomerular filtration rate based on locally measured creatinine levels.

Table S4: Multivariate adjusted logistic regression analysis of factors associated with a rapid decline in kidney function at baseline among apparently healthy young males

Factors	Figure 2A								Figure 2B			
	Model 3 without uNGAL levels (n=78)				Model 4 with uNGAL levels (n=78)				Model 5 without uNGAL levels (n=67)			
	Coefficient	SE	95% CI	P-value	Coefficient	SE	95% CI	P-value	Coefficient	SE	95% CI	P-value
Age	-0.06	0.06	-0.19 to 0.06	0.354	-0.06	0.06	-0.20 to 0.06	0.327	-0.11	0.09	-0.29 to 0.05	0.187
Season												
Summer	0	--	--	--	0	--	--	--	0	--	--	--
Winter	1.00				1.00				1.00			
Outdoor work												
Yes	1.59	1.08	-0.54 to 3.72	0.144	1.77	1.10	-0.39 to 3.94	0.110	1.42	1.12	-0.78 to 3.63	0.206
No	1.00				1.00				1.00			
Urinary ACR												
≥30 mg/g	0	--	--	--	0	--	--	--	0	--	--	--
<30 mg/g	1.00				1.00				1.00			
Urinary NGAL	-	-	-	-	0.97	0.49	-0.0008 to 1.94	0.050	-	-	-	-
eGFR$_{Scr}$ at baseline	-0.004	0.01	-0.03 to 0.02	0.789	-0.004	0.01	-0.03 to 0.02	0.794	-0.02	0.02	-0.06 to 0.01	0.237
eGFR$_{Scr}$ at second study visit	-	-	-	-	-	-	-	-	-0.06	0.02	-0.11 to -0.01	0.018
eGFR$_{Scr}$ at third study visit	-	-	-	-	-	-	-	-	-	-	-	-

Abbreviations: SE: standard error, UACR: urinary albumin creatinine ratio, uNGAL: urinary neutrophil gelatinase-associated lipocalin, eGFR$_{Scr}$: estimated glomerular filtration rate based on locally measured creatinine levels.

Continued: Table S4: Multivariate adjusted logistic regression analysis of factors associated with a rapid decline in kidney function at baseline among apparently healthy young males

Factors	Figure 2B				Figure 2C							
	Model 6 with uNGAL levels (n=67)				Model 7 without uNGAL levels (n=72)				Model 8 with uNGAL levels (n=72)			
	Coefficient	SE	95% CI	P-value	Coefficient	SE	95% CI	P-value	Coefficient	SE	95% CI	P-value
Age	-0.11	0.08	-0.29 to 0.06	0.202	-0.18	0.10	-0.38 to 0.01	0.068	-0.18	0.09	-0.37 to 0.01	0.066
Season												
Summer	0	--	--	--	0	--	--	--	0	--	--	--
Winter	1.00				1.00				1.00			
Outdoor work												
Yes	1.48	1.13	-0.73 to 3.71	0.190	3.12	2.01	-0.81 to 7.07	0.120	3.35	2.14	-0.84 to 7.55	0.117
No	1.00				1.00				1.00			
Urinary ACR												
≥30 mg/g	0	--	--	--	0	--	--	--	0	--	--	--
<30 mg/g	1.00				1.00				1.00			
Urinary NGAL	0.63	0.62	-0.58 to 1.84	0.310	-	-	-	-	0.76	0.63	-0.48 to 2.01	0.229
eGFR$_{Scr}$ at baseline	-0.02	0.02	-0.06 to 0.01	0.243	-0.0001	0.01	-0.03 to 0.03	0.996	0.0006	0.01	-0.03 to 0.03	0.972
eGFR$_{Scr}$ at second study visit	-0.05	0.02	-0.10 to -0.004	0.034	-	-	-	-	-	-	-	-
eGFR$_{Scr}$ at third study visit	-	-	-	-	-0.07	0.02	-0.11 to -0.03	<0.001	-0.07	0.02	-0.11 to -0.03	<0.001

Abbreviations: SE: standard error, uNGAL: urinary neutrophil gelatinase-associated lipocalin, UACR: urinary albumin creatinine ratio, eGFR$_{Scr}$: estimated glomerular filtration rate based on locally measured creatinine levels.

Continued: Table S4: Multivariate adjusted logistic regression analysis of factors associated with a rapid decline in kidney function at baseline among apparently healthy young males

Factors	Figure 2D							
	Model 9 without uNGAL levels (n=66)				Model 10 with uNGAL levels (n=66)			
	Coefficient	SE	95% CI	P-value	Coefficient	SE	95% CI	P-value
Age	-0.25	0.12	-0.50 to 0.002	0.053	-0.23	0.12	-0.49 to 0.01	0.065
Season								
Summer	0	--	--	--	0	--	--	--
Winter	1.00				1.00			
Outdoor work								
Yes	3.40	2.24	-1.00 to 7.81	0.130	3.47	2.29	-1.02 to 7.97	0.130
No	1.00				1.00			
Urinary ACR								
≥30 mg/g	0	--	--	--	0	--	--	--
<30 mg/g	1.00				1.00			
Urinary NGAL	-	-	-	-	0.42	0.73	-1.01 to 1.86	0.561
eGFR$_{Scr}$ at baseline	-0.02	0.02	-0.07 to 0.01	0.239	-0.02	0.02	-0.06 to 0.01	0.254
eGFR$_{Scr}$ at second study visit	-0.03	0.02	-0.08 to 0.02	0.269	-0.02	0.02	-0.08 to 0.03	0.360
eGFR$_{Scr}$ at third study visit	-0.08	0.02	-0.12 to -0.03	0.001	-0.07	0.02	-0.12 to -0.03	0.001

Abbreviations: SE: standard error, uNGAL: urinary neutrophil gelatinase-associated lipocalin, UACR: urinary albumin creatinine ratio, eGFR$_{Scr}$: estimated glomerular filtration rate based on locally measured creatinine levels.

Figure S2: ROC curves for the model predicting stable kidney function versus established renal dysfunction. The 95% confidence intervals for the ROC curves (0.5) are displayed.
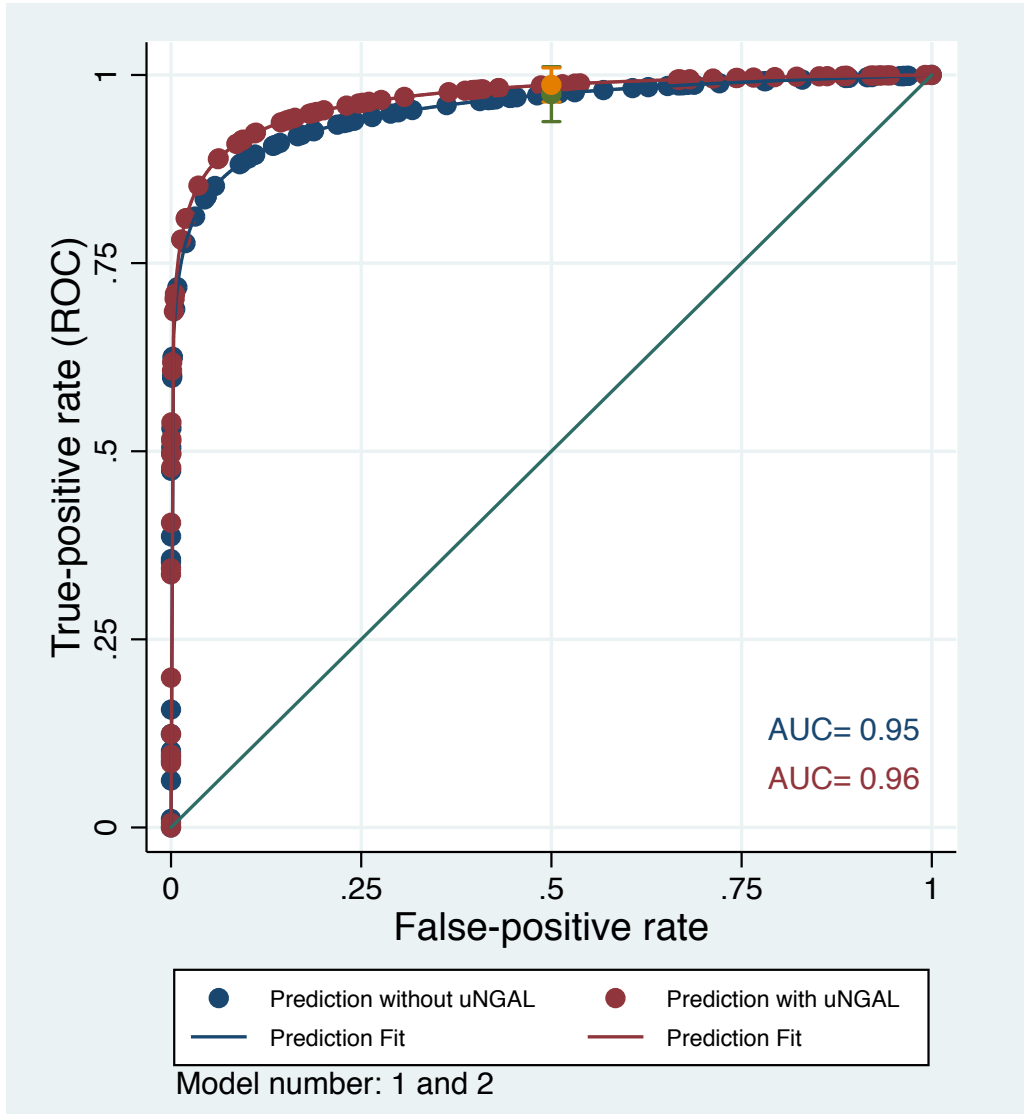
Figure S3: ROC curves for the model predicting stable kidney function versus a rapid decline in kidney function. The 95% confidence intervals for ROC curves (0.5) are displayed.

A. Visit 1

AUC= 0.63
AUC= 0.70

Prediction without uNGAL   Prediction with uNGAL
Prediction Fit   Prediction Fit

Model number: 3 and 4

B. Visit 1&2

AUC= 0.73
AUC= 0.75

Prediction without uNGAL   Prediction with uNGAL
Prediction Fit   Prediction Fit

Model number: 5 and 6

C. Visit 1&3

AUC= 0.82
AUC= 0.83

Prediction without uNGAL   Prediction with uNGAL
Prediction Fit   Prediction Fit

Model number: 7 and 8

D. Visit 1 to 3

AUC= 0.87
AUC= 0.87

Prediction without uNGAL   Prediction with uNGAL
Prediction Fit   Prediction Fit

Model number: 9 and 10