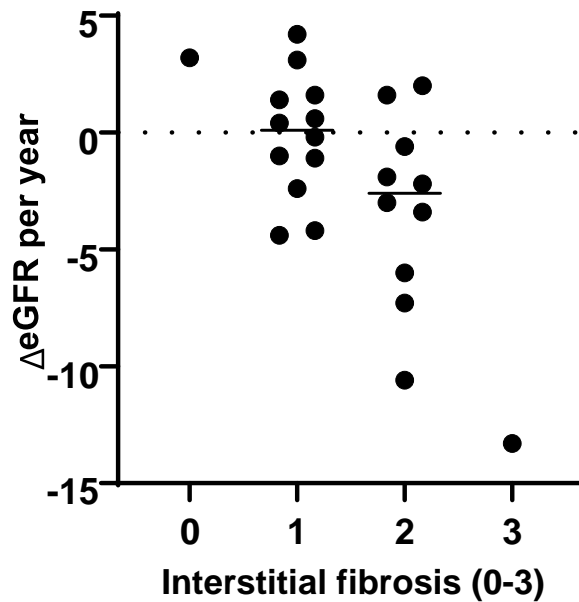
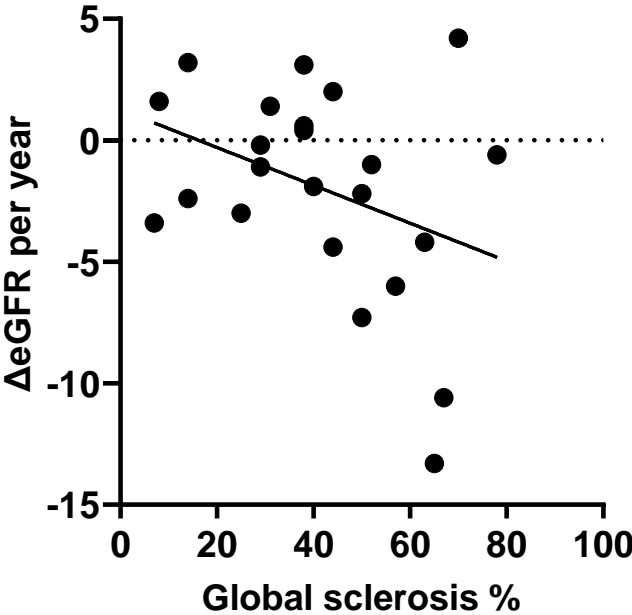


**Figure S1:** Interstitial fibrosis at baseline and change in eGFR. The degree of interstitial fibrosis at the time of the biopsy is significantly correlated with a decline in eGFR. One-way ANOVA,  $F(3,20)=6.397$ ,  $p=0.003$ . Graph shows individual values and median. Semi-quantification of interstitial fibrosis in the cortical area defined as: 0= no fibrosis; 1=  $\leq 25\%$  fibrosis; 2= 26-50% fibrosis; 3> 50% fibrosis.



**Figure S2:** Percentage of glomerulosclerosis at baseline and change in eGFR. The percentage of glomerulosclerosis at the time of the biopsy shows a tendency, but non-significant association with a decline in eGFR. Linear regression,  $p=0.09$ .



**Table S1:** Individual biochemical follow-up data of two patient case series with Mesoamerican Nephropathy from El Salvador and Nicaragua 4-7 years (F2) after kidney biopsy study.

Pat no	eGFR T0	eGFR F2	Follow- up time T0-F2	$\Delta$ eGFR per year	S-Na T0	S-Na F2	S-K T0	S-K F2	S- Mg T0	S-Mg F2 <sup>a</sup>	ACR T0	ACR F2	24h- U T0 <sup>b</sup>
ES-1	62	34	3.8	-7.3	142	139	3.9	3.4 <sup>c</sup>	1.34 <sup>c</sup>	-	2	-/ <sup>d</sup>	-
ES-2	30	5	1.6	-13.3	139	139	5.3	3.4 <sup>c</sup>	1.8	-	788	-/ <sup>d</sup>	7.5
ES-3	40	61	6.8	3.1	137	137	4.1	3.6	2.02	-	6	-/ <sup>d</sup>	-
ES-4	43	30	6.8	-1.9	140	138	3.4 <sup>c</sup>	2.8 <sup>c</sup>	1.26 <sup>c</sup>	-	8	-/ <sup>d</sup>	-
ES-5	78	48	6.8	-4.4	137	136	2.6 <sup>c</sup>	2.4 <sup>c</sup>	0.88 <sup>c</sup>	-	7	-/ <sup>d</sup>	-
ES-6	28	24	7.0	-0.6	141	139	4.1	3.8	1.58	-	12	-/ <sup>d</sup>	-
ES-7	75	68	6.7	-1.1	139	137	3.6	3.3 <sup>c</sup>	1.22 <sup>c</sup>	-	17	-/ <sup>d</sup>	2.5
Nic-1	53	32	5.0	-4.2	134	136	4.4	5.7	1.46	1.82	5	18	3.2
Nic-2	49	57	5.0	1.6	138	140	3.2 <sup>c</sup>	4.3	1.26 <sup>c</sup>	1.42	1	13	2.0
Nic-3	50	71	5.0	4.2	135	139	3.5	4.7	1.20 <sup>c</sup>	1.04 <sup>c</sup>	3	5	1.9

<b>Nic-4</b>	39	49	5.0	2.0	138	138	3.6	4.2	1.38 <sup>c</sup>	1.46	4	31	2.5
<b>Nic-5</b>	44	27	5.0	-3.4	137	140	3.8	4.7	1.08 <sup>c</sup>	1.08 <sup>c</sup>	2	35	3.5
<b>Nic-6</b>	84	91	5.0	1.4	136	136	4.9	3.4 <sup>c</sup>	1.56	1.78	1	10	3.0
<b>Nic-7</b>	54	53	5.0	-0.2	135	137	2.2 <sup>c</sup>	4.8	1.50	1.48	317	18	5.3
<b>Nic-8</b>	56	59	5.0	0.6	136	141	4.7	5.1	1.46	1.40	8	30	1.6
<b>Nic-9</b>	74	62	5.0	-2.4	137	141	3.8	5.1	1.62	1.60	9	13	3.7
<b>Nic-10</b>	81	97	5.0	3.2	137	139	4.5	4.7	1.58	1.80	1	8	1.3
<b>Nic-11</b>	79	72	5.0	-1.4	137	139	3.7	4.3	1.58	1.76	2	7	3.7
<b>Nic-12</b>	33	22	5.0	-2.2	136	139	3.6	4.1	1.02 <sup>c</sup>	0.98 <sup>c</sup>	3	9	4.8
<b>Nic-13</b>	61	63	5.0	0.4	138	138	3.6	4.7	1.60	1.30 <sup>c</sup>	2	30	3.2
<b>Nic-14</b>	42	44	5.0	0.4	137	139	3.1 <sup>c</sup>	4.0	1.10 <sup>c</sup>	1.04 <sup>c</sup>	1	8	1.7
<b>Nic-15</b>	41	11	5.0	-6.0	133	137	4.3	3.9	1.02 <sup>c</sup>	1.30 <sup>c</sup>	29	14	2.1
<b>Nic-16</b>	43	51	5.0	1.6	139	139	3.7	4.4	1.64	1.66	2	60	2.8
<b>Nic-17</b>	51	46	5.0	-1.0	139	138	4.2	4.6	1.54	1.64	7	7	3.6
<b>Nic-18</b>	96	81	5.0	-3.0	136	136	3.8	4.5	1.62	1.50	13	6	6.7

<b>Nic-19</b>	60	7	5.0	-10.6	136	139	3.3 <sup>c</sup>	5.0	1.50	2.46	809	143	2.2
<b>Mean</b>	<b>56</b>	<b>49</b>	<b>5.2</b>	<b>-1.7</b>	<b>137</b>	<b>138</b>	<b>3.8</b>	<b>4.2</b>	<b>1.42</b>	<b>1.50</b>	<b>79</b>	<b>25</b>	<b>3.3</b>
<b>SD</b>	<b>18</b>	<b>23</b>	<b>1.1</b>	<b>4.1</b>	<b>2</b>	<b>1</b>	<b>0.7</b>	<b>0.8</b>	<b>0.27</b>	<b>0.36</b>	<b>220</b>	<b>32</b>	<b>1.6</b>
<b>Unit</b>	ml/min/1.73m <sup>2</sup>	years	ml/min/ 1.73m <sup>2</sup> /year	mEq/ L	mEq /L	mEq/ L	mEq/ L	mEq/L	mEq/L	mEq/L	mEq/ L	mg/g	L

Abbreviations: T0, baseline; F2, second follow-up;  $\Delta$  eGFR, change in eGFR; S-Na, serum sodium; S-K, serum potassium; ACR, urine albumin creatinine ratio; 24h-U, 24-hour urine; SD, standard deviation.

Reference values: S-Na, 137-145 mEq/L; S-K, 3.5-5.0 mEq/L; S-Mg, 1.40-1.90 mEq/L; UACR, <30 mg/g.

Conversion factors for units: ACR in mg/g to mg/mmol,  $\times 0.113$ .

<sup>a</sup> S-Mg at follow-up not available in patients from El Salvador.

<sup>b</sup> 24-hour urine collection only available in two patients from El Salvador.

<sup>c</sup> Below reference value.

<sup>d</sup> Incomplete data.

**Table S2:** Baseline eGFR, progression rate, and kidney biopsy findings at baseline in two patient case series with Mesoamerican Nephropathy from El Salvador and Nicaragua.

Pat no	eGFR T0	$\Delta$ eGFR per year	Global scleros (%) <sup>a</sup>	Segm scleros (0-1) <sup>b</sup>	Interst fibrosis (0-3) <sup>c</sup>	Interst inflam (0-3) <sup>c</sup>	Tubular atrophy (0-3) <sup>c</sup>	Glom size (0-3) <sup>d</sup>	Wrinkl GBM/ Periglom fibrosis (0-1) <sup>e</sup>
ES-1	62	-7.3	50%	0	2	1	1	2	1
ES-2	30	-13.3	65%	1	3	2	2	3	1
ES-3	40	3.1	38%	0	1	1	1	1	1
ES-4	43	-1.9	40%	0	2	2	2	2	1
ES-5	78	-4.4	44%	0	1	1	1	1	1
ES-6	28	-0.6	78%	1	2	1	2	3	1
ES-7	75	-1.1	29%	0	1	0	1	1	1
Nic-1	53	-4.2	63%	0	1	1	1	3	1
Nic-2	49	1.6	n/a <sup>f</sup>	0	1	1	0	1	0

<b>Nic-3</b>	50	4.2	70%	0	1	1	1	2	1
<b>Nic-4</b>	39	2.0	44%	0	2	2	2	2	1
<b>Nic-5</b>	44	-3.4	7%	0	2	1	1	3	1
<b>Nic-6</b>	84	1.4	31%	0	1	1	1	2	1
<b>Nic-7</b>	54	-0.2	29%	1	1	1	1	3	1
<b>Nic-8</b>	56	0.6	38%	0	1	1	1	3	1
<b>Nic-9</b>	74	-2.4	14%	0	1	1	1	2	1
<b>Nic-10</b>	81	3.2	14%	0	0	0	0	2	0
<b>Nic-11</b>	79	-1.4	n/a <sup>f</sup>	-	-	-	-	-	-
<b>Nic-12</b>	33	-2.2	50%	0	2	2	1	2	1
<b>Nic-13</b>	61	0.4	38%	0	1	0	1	2	1
<b>Nic-14</b>	42	0.4	n/a <sup>f</sup>	-	-	-	-	-	-
<b>Nic-15</b>	41	-6.0	57%	1	2	1	2	2	1
<b>Nic-16</b>	43	1.6	8%	0	2	1	1	2	1
<b>Nic-17</b>	51	-1.0	52%	0	1	1	1	2	1

<b>Nic-18</b>	96	-3.0	25%	0	2	1	1	2	1
<b>Nic-19</b>	60	-10.6	67%	0	2	1	1	3	1
<b>Unit</b>		ml/min/1.73m <sup>2</sup> /year							

eGFR T0 and kidney biopsy findings compiled from baseline studies (Wijkström et al, *Am J Kidney Dis* 2013 and Wijkström et al, *Am J Kidney Dis* 2017).

Abbreviations: T0, baseline;  $\Delta$  eGFR, change in eGFR; Global sclerosis, globally sclerosed glomeruli; Segm Sclerosis, segmental sclerosed glomeruli; Interst fibrosis, interstitial fibrosis; Interst inflam, interstitial inflammation; Glom size, glomerular size; Wrinkl GBM, wrinkled glomerular basement membrane; Periglom fibrosis, periglomerular fibrosis.

<sup>a</sup> Percentage of globally sclerosed glomeruli in the biopsy

<sup>b</sup> 0=No segmentally sclerosed glomeruli; 1=presence of segmentally sclerosed glomeruli in the biopsy.

<sup>c</sup> Grading of interstitial fibrosis, interstitial inflammation, and tubular atrophy is defined as 0=no; 1=mild, affecting 25% of the area; 2=moderate, affecting 26-50%; and 3=severe, affecting > 50%.

<sup>d</sup> Grading 0=normal, 1=mild hypertrophy; 2=moderate; and 3=severe hypertrophy.

<sup>e</sup> 0=No; 1=Yes.

<sup>f</sup> Not applicable, not enough tissue for evaluation (less than 5 glomeruli in biopsy).



**Table S3:** Self-reported data of medication and work exposure during follow-up in the 19 patients with Mesoamerican Nephropathy from Nicaragua.

<b>Pat no</b>	<b>eGFR T0</b>	<b>ΔeGFR per year</b>	<b>ACEi/ ARBs</b>	<b>Allo-purinol</b>	<b>Physical demanding work last 3 months</b>	<b>Agricultural work tasks last 5 years<sup>a</sup></b>	<b>Exposure to agrochemicals last 3 years?<sup>b</sup></b>
<b>Nic-1</b>	53	-4.2	No	Yes	Yes	Yes	Yes
<b>Nic-2</b>	49	1.6	Yes	Yes	Yes	Yes	No
<b>Nic-3</b>	50	4.2	Yes	Yes	Yes	Yes	Yes
<b>Nic-4</b>	39	2.0	No	No	No	No	No
<b>Nic-5</b>	44	-3.4	No	No	No	No	No
<b>Nic-6</b>	84	1.4	No	No	No	Yes	No
<b>Nic-7</b>	54	-0.2	No	No	No	Yes	Yes
<b>Nic-8</b>	56	0.6	No	Yes	No	Yes	No
<b>Nic-9</b>	74	-2.4	No	Yes	No	Yes	Yes
<b>Nic-10</b>	81	3.2	Yes	Yes	No	No	No

<b>Nic-11</b>	79	-1.4	Yes	Yes	Yes	No	Yes
<b>Nic-12</b>	33	-2.2	Yes	Yes	No	No	No
<b>Nic-13</b>	61	0.4	Yes	Yes	No	No	No
<b>Nic-14</b>	42	0.4	Yes	No	No	No	No
<b>Nic-15</b>	41	-6.0	Yes	Yes	No	Yes	No
<b>Nic-16</b>	43	1.6	No	Yes	Yes	Yes	Yes
<b>Nic-17</b>	51	-1.0	No	Yes	No	Yes	No
<b>Nic-18</b>	96	-3.0	Yes	Yes	Yes	Yes	Yes
<b>Nic-19</b>	60	-10.6	Yes	No	Yes	No	No

Abbreviations:  $\Delta$  eGFR, change in eGFR; ACEi/ARBs, Angiotensin converting enzyme inhibitors/ Angiotensin II receptor blockers.

<sup>a</sup> Among patients with agricultural work tasks during follow-up, the median duration was 3.0 years (range 0.3-5 years). Only 1 patient worked with sugarcane. Subsistence farming was the most common work task, reported from 6 patients.

<sup>b</sup> Agrochemicals reported were: 2,4D (2,4-Dichlorophenoxyacetic acid) in two patients; Atrazine in two patients; Chlorothalonil in one patient; Chlorpyrifos in one patient; Cypermethrin in four patients; Diphacinone in one patient; Glyphosate in four patients; Paraquat in one patient.