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Survey for dialysis patients

Supplemental Methods

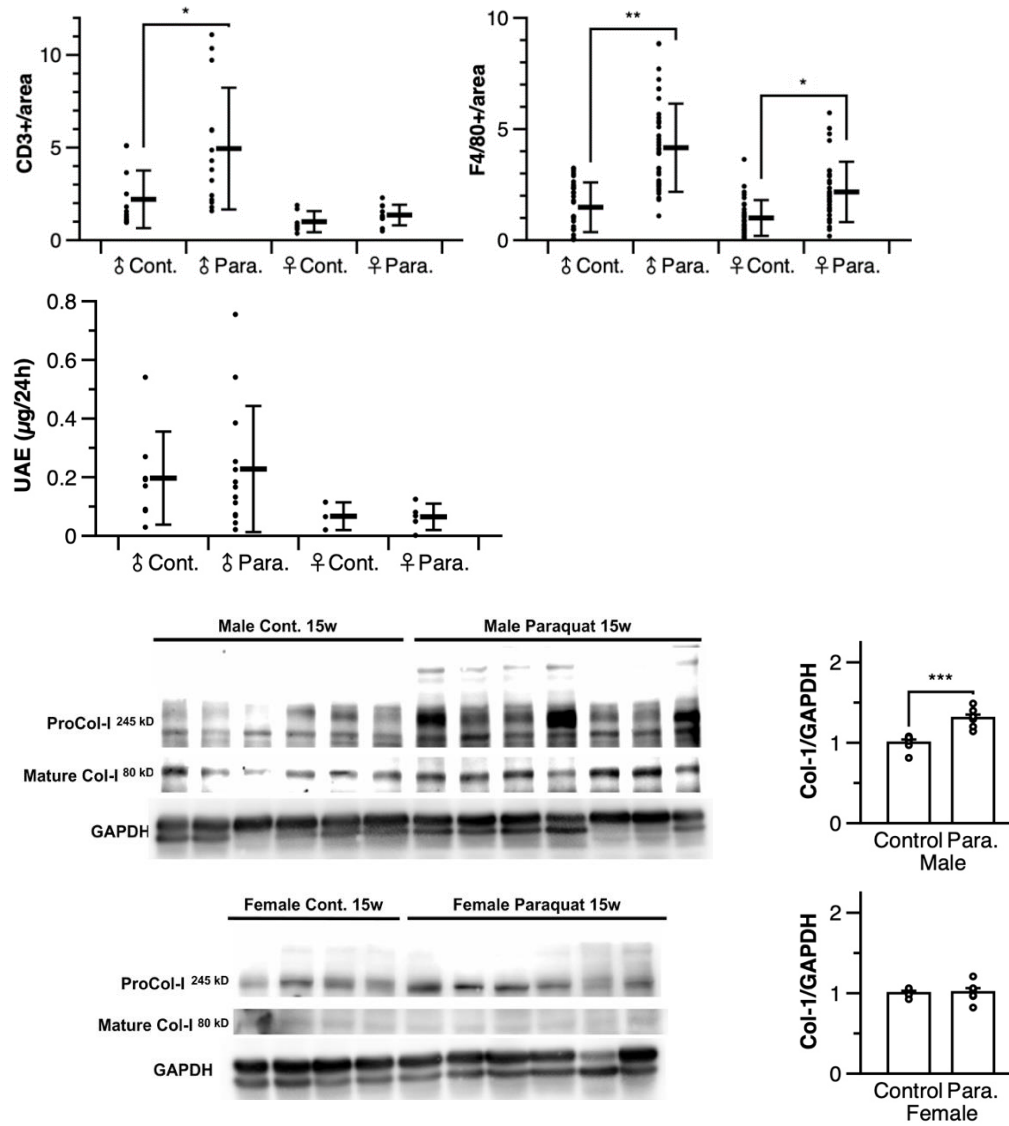
Reactive oxygen species assay

BUMPT cells were obtained from Dr. Zheng of Augusta University and cultured as previously described (1). Cells seeded on poly-L-lysine-coated cover slips were treated with either paraquat (5 μ M) or vehicle for 16 hours. MitoSOX (ThermoFisher) staining was performed as previously described (2) and fluorescence (integrated density) per cell was quantified for each high power field (HPF, at 20x) using ImageJ software. Samples were prepared in triplicates and 3 HPF were counted per sample. Relative MitoSOX intensity was analyzed using Student's T-test.

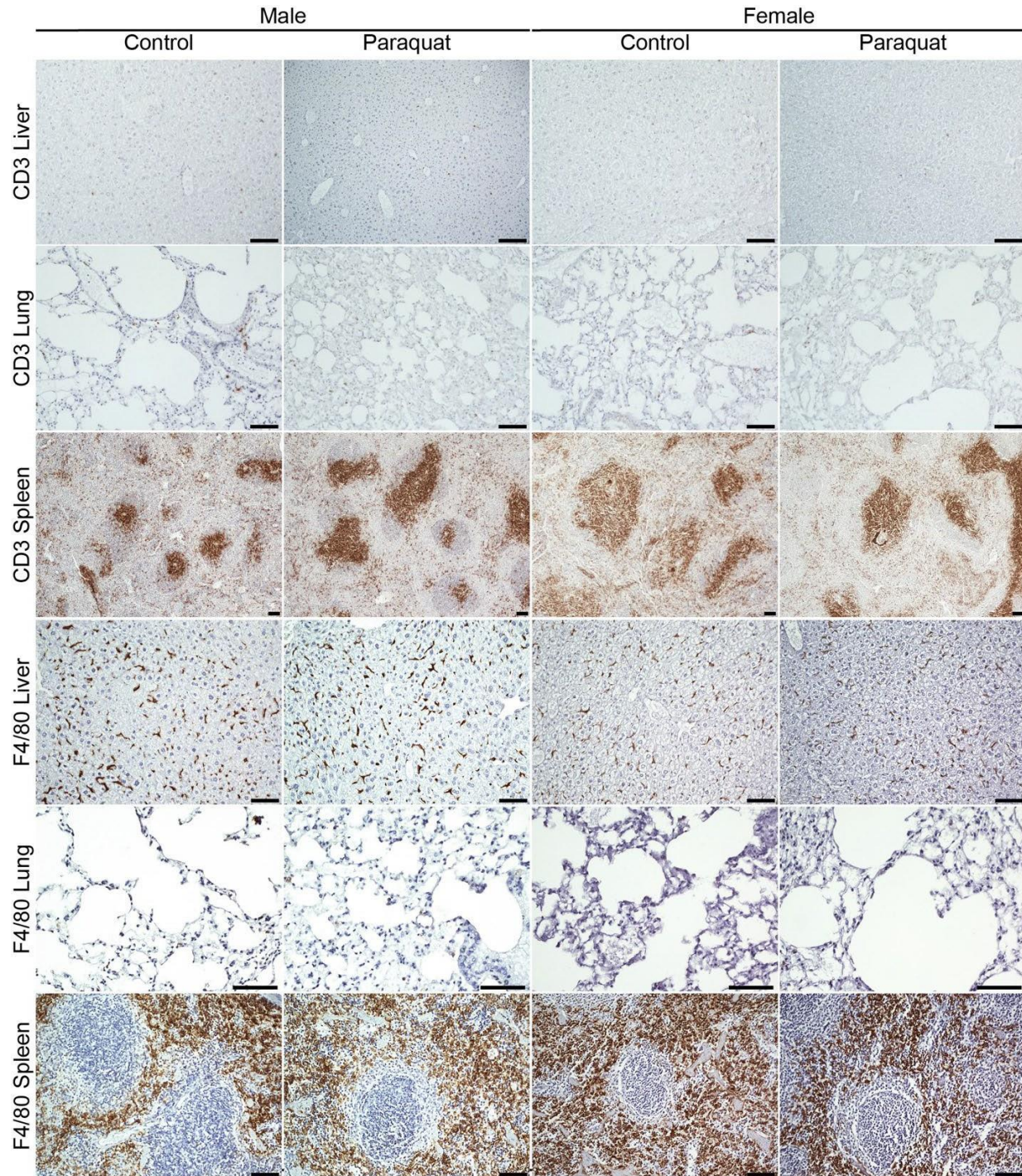
Western blotting

Total mouse kidney lysates were prepared and analyzed by Western blot as previously described (2). Briefly, protein concentrations were determined using BCA assay kit (ThermoFisher, Waltham, MA). Samples were prepared using Laemmli sample buffer (Bio-rad, Hercules, CA) and dithiothreitol (Sigma-Aldrich); samples used for collagen-I detection were not reduced or boiled. Tris-glycine gels (8%) with and without SDS were used for OCT2/MATE-1 and Col1, respectively. Proteins were transferred to nitrocellulose membrane using the Trans-Blot Turbo Transfer System (Bio-rad). Primary antibodies included anti-collagen I (Novus Biologicals, Centennial, CO), anti-OCT2 (Abcam), anti-MATE-1 (Biorbyt, St. Louis, MO) anti-beta actin (Bio-rad) and anti-GAPDH (Millipore Sigma, Burlington, MA).

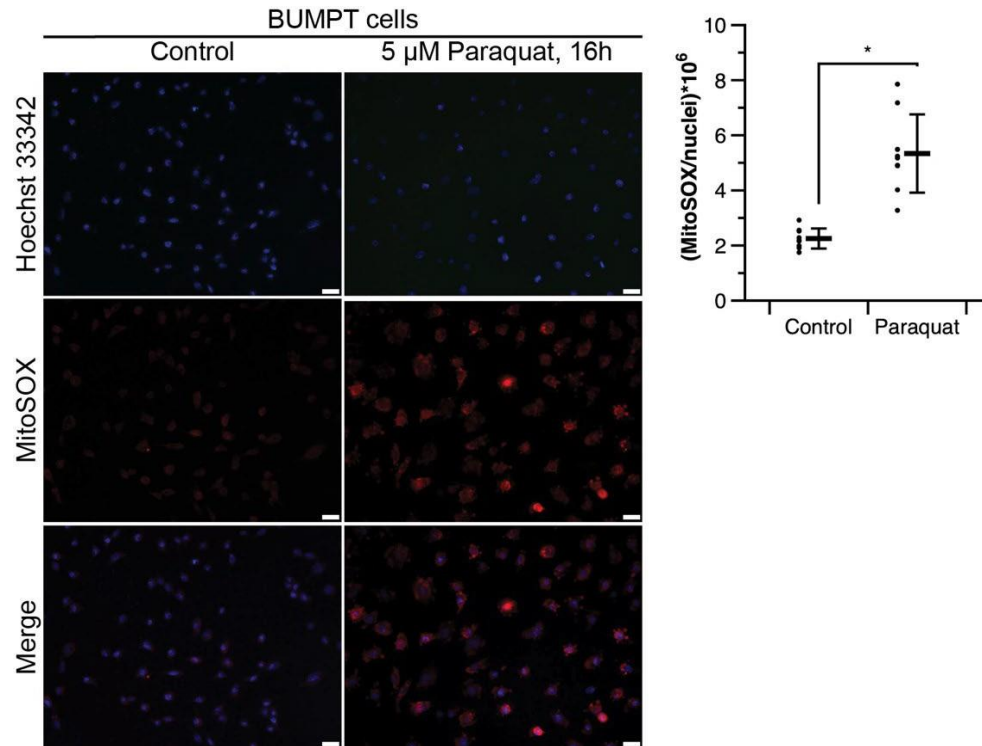
1. Zheng M, Cai J, Liu Z, Shu S, Wang Y, Tang C, Dong Z: Nicotinamide reduces renal interstitial fibrosis by suppressing tubular injury and inflammation. *J Cell Mol Med*, 23: 3995-4004, 2019
2. Luping H, Tatiana B, Minyi C, Gabriel D, Dajun L, David S-H: Overexpression of stanniocalcin-1 inhibits reactive oxygen species and renal ischemia/reperfusion injury in mice. *Kidney International*, 82: 867-877, 2012



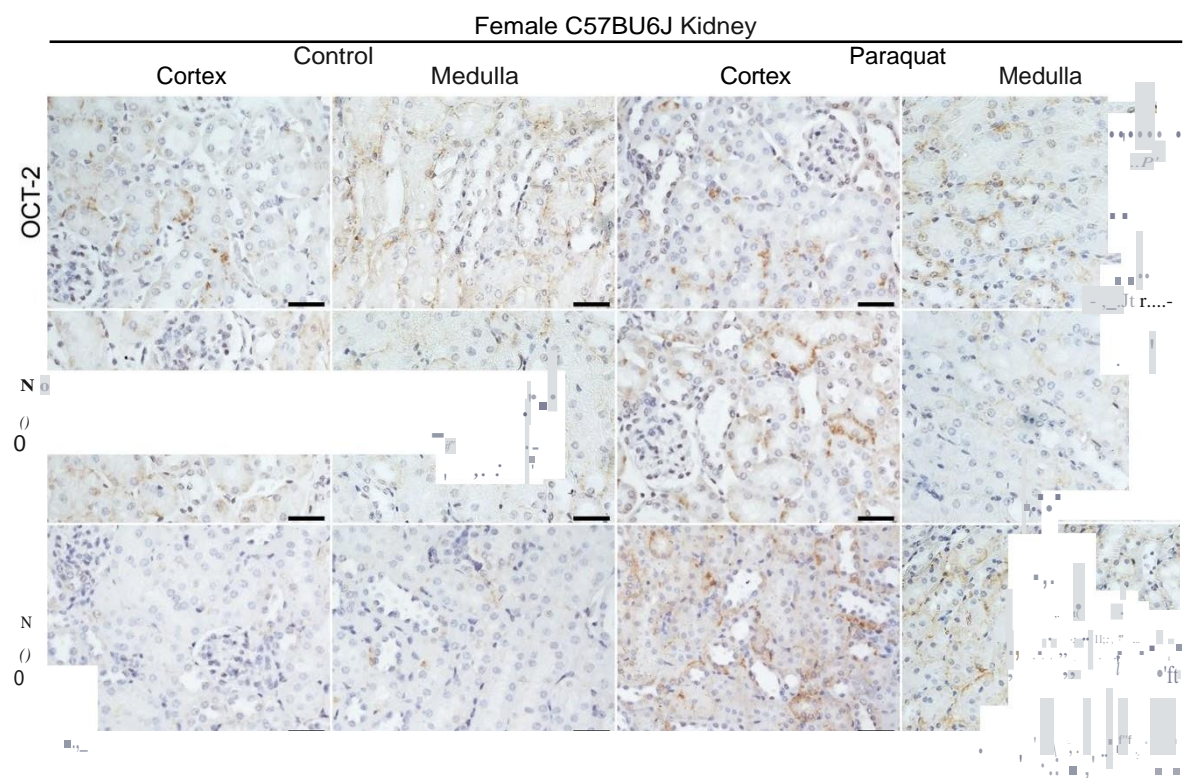
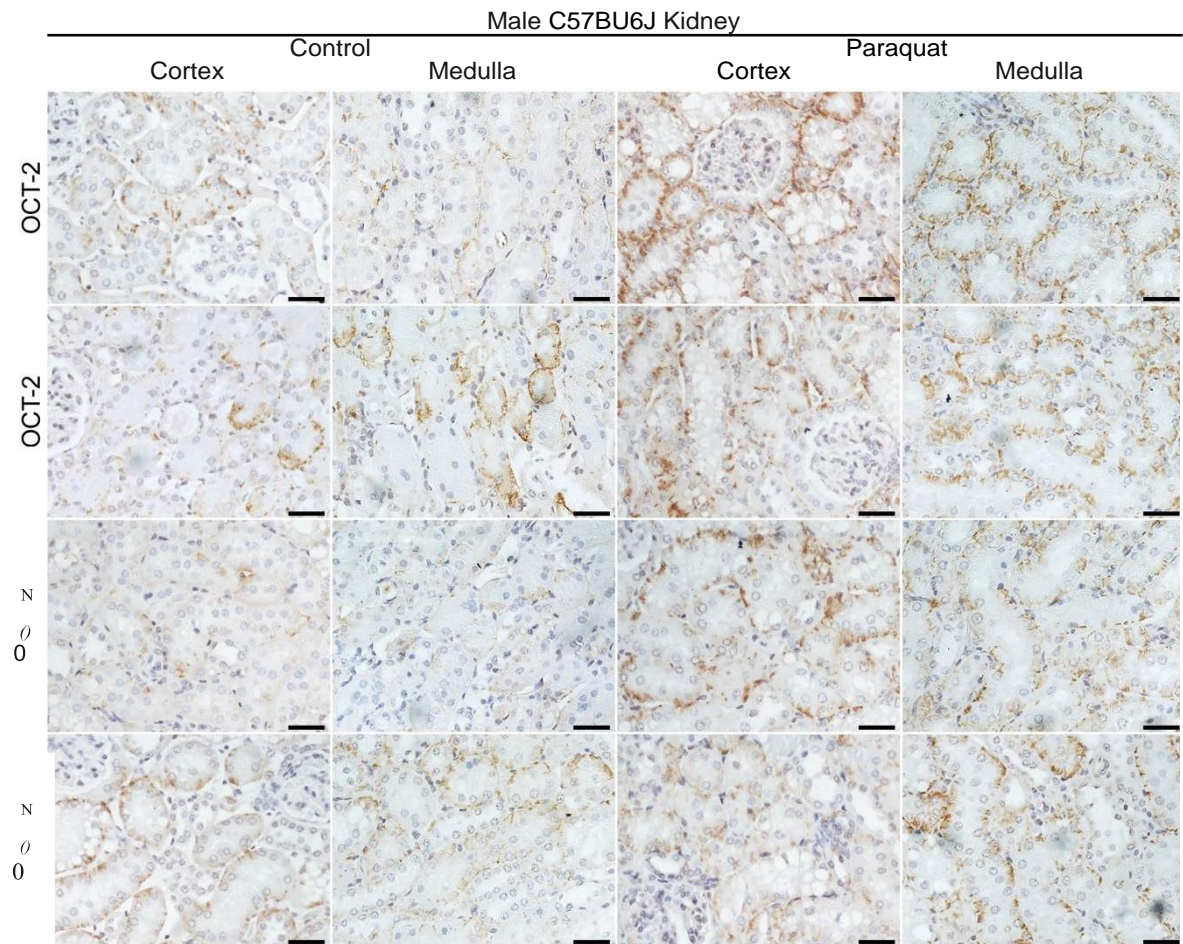
Supplemental Figure 1. CD3 and F4/80 immunohistochemical staining, albuminuria and collagen-1 expression in paraquat versus control treated mice. *Upper*, Quantification of CD3+ and F4/80+ immunohistochemical staining at 10 weeks in kidney tissue of paraquat-treated versus saline-treated mice; Data are plotted as positively stained area/cells normalized to female control; * P, <0.01. **, P< 0.001. Female mice displayed 1.3-fold (p=0.4) and 2.3-fold (p<0.01) increase in CD3 and F4/80, respectively. Error bars represent SD. *Middle*, urine collection over 12 hours was performed at completion of 15 weeks of either saline or paraquat (20 mg/kg) injections, and urine albumin was measured by ELISA. No difference was observed in males or females treated with paraquat versus saline. *Lower*, collagen type-I detected by Western blot in whole kidney lysates of male and female mice treated for 15 weeks with paraquat versus saline. Both procollagen and mature collagen bands were used in quantitation. GAPDH utilized as loading control. Adjacent graphs depict the means \pm SEM of quantified collagen I expression normalized to GAPDH; ***, P < 0.001.



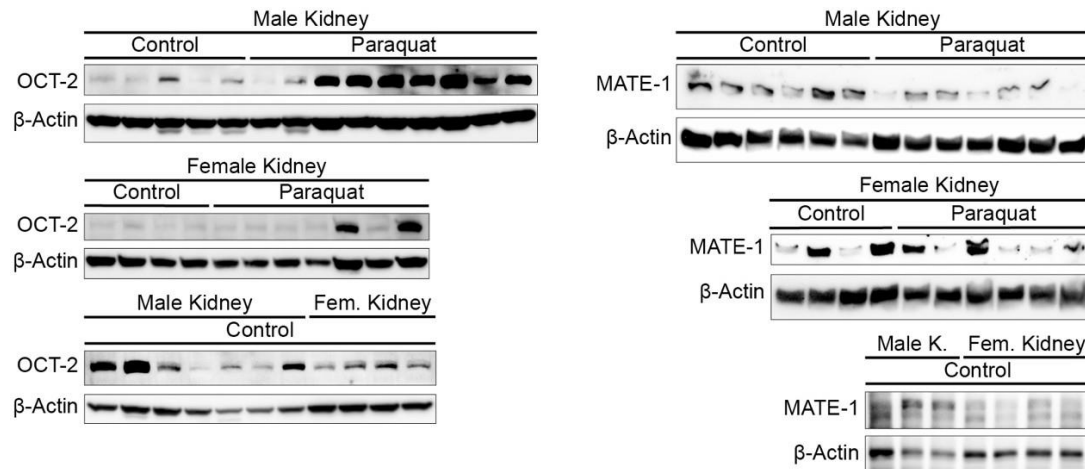
Supplemental Figure 2. Lung, liver and spleen histology of paraquat versus vehicle treated control mice. Representative immunohistochemical staining of CD3 and F4/80 in indicated organ sections from mice treated with paraquat or saline for 10 weeks. No differences were observed in CD3 or F4/80 staining in liver or lung. Scale bars are 50 μ m.



Supplemental Figure 3. *In vitro* reactive oxygen species generation in BUMPT cells with paraquat-treatment. Representative micrographs of BUMPT mouse proximal tubule cells treated for 16 hours with paraquat (5 μ M) or vehicle and stained with Hoechst 33342 (DNA) and MitoSOX, a mitochondrial superoxide indicator; scale bars 25 μ m. Three replicates per treatment were imaged with 3 HPF each, and MitoSOX signal was quantified in ImageJ and normalized to number of nuclei. Bar is average, error bars are standard deviation; *, $P < 0.001$.



Supplemental Figure 4. OCT-2 staining of male and female mice treated with paraquat or vehicle control. Fixed paraffin-embedded kidney sections from male and female mice treated for 15 weeks with either paraquat or saline were immunostained for organic cation transporter-2 (OCT-2). Samples counterstained with hematoxylin; scale bar 25 μm , zoomed. Although MATE-1 expression in mouse kidney lysates was measured using Western blot, the antibody was not suitable for IP use in mice.



Supplemental Figure 5. Western blots of total kidney lysates from paraquat or control mice probed for OCT-2 and MATE-1.

Total kidney lysates from male and female mice treated with paraquat or saline for 15 weeks were analyzed by Western blot with indicated primary antibodies. Kidney OCT2 expression was higher ($P < 0.01$) in male versus female mice. Paraquat treated male mice had higher ($P < 0.02$) kidney OCT-2 expression than control male mice at 15 weeks. MATE-1 kidney expression decreased ($P < 0.03$) in paraquat-treated male mice relative to saline-treated control.

Supplemental Table 1A

Characteristics among Mesoamerican nephropathy-kidney failure patients and non-Mesoamerican nephropathy-kidney failure patients.

Characteristic	Mesoamerican nephropathy-kidney failure (N=52)	Kidney failure from other causes (N=63)	p-value
Age*	38.0 (30.0,46.0) 22 - 60	45.0 (38.0,51.0) 25 - 73	<0.001
Age when moved to US*	21.5 (15.5,28.0) 1 - 46	22.0 (18.0,28.0) 5 - 62	0.44
US-Farming years*	0.0 (0.0,0.0) 0 - 5	0.0 (0.0,0.0) 0 - 4	0.52
US-Construction years*	0.3 (0.0,3.0) 0 - 20	0.0 (0.0,3.0) 0 - 30	0.33
US-Landscaping years*	0.0 (0.0,0.5) 0 - 12	0.0 (0.0,0.0) 0 - 13	0.036
Duration (years) farming in origin country* ^[1]	5.0 (0,12) 0 - 34	0 (0,4) 0 - 49	<0.001
[N of missing]	0	1	
Agrochemical exposure duration* ^[2]	3.5 (0.0,10.0) 0 - 23	0.0 (0.0,0.0) 0 - 20	<0.001
[N of missing]	2	0	
Agrochemical exposure episodes* ^[3]	9.0 (0.0,160.0) 0 - 4745	0.0 (0.0,0.0) 0 - 50	<0.001
[N of missing]	6	5	
Years in Houston*	13.5 (8.5,20.0) 1 - 30	20.0 (13.0,24.0) 3 - 43	0.008
Gender			
Female	2 (3.8)	29 (46.0)	<0.001
Male	50 (96.2)	34 (54.0)	
Origin country locale			
City	16 (30.8)	25 (39.7)	0.32
Village/farm	36 (69.2)	38 (60.3)	
Highest education achieved			
Some school	40 (81.6)	34 (59.6)	0.02
High school	6 (12.2)	20 (35.1)	
College	3 (6.1)	3 (5.3)	
[N of missing]	3	6	
Literate	49 (94.2)	57 (90.5)	
English - Second Language	19 (36.5)	16 (25.4)	
First degree relative with renal dx	11 (21.2)	9 (14.3)	
Diabetes mellitus	0 (0.0)	18 (28.6)	
Hypertension	0 (0.0)	44 (69.8)	
Herb/alternative medication use	4 (7.7)	1 (1.6)	0.17
Analgesic use	19 (36.5)	15 (23.8)	0.14
NSAID use	5 (9.6)	9 (14.3)	0.46
Drug allergies	12 (23.1)	17 (27.0)	0.63
Currently employed	22 (42.3)	18 (28.6)	
US Farming	4 (7.7)	3 (4.8)	0.7
US Construction	30 (57.7)	24 (38.1)	0.04
US Landscaping	20 (38.5)	11 (17.5)	0.01
Farming in origin country	37 (71.2)	20 (31.7)	<0.001
Cane Cutter	7 (13.5)	8 (12.7)	0.9

Characteristic	Mesoamerican nephropathy-kidney failure (N=52)	Kidney failure from other causes (N=63)	p-value
Cotton/Corn	32 (61.5)	17 (27.0)	<0.001
Animals	17 (32.7)	10 (15.9)	0.03
Other produce	20 (38.5)	18 (28.6)	0.26
Lived in another U.S. city	16 (30.8)	18 (30.0)	0.9
	0	3	
Country of origin - climate hot	37 (71.2)	38 (60.3)	0.23
Hydrates while working	46 (88.5)	52 (82.5)	0.37
Drank well water at work or home	33 (63.5)	17 (27.0)	<0.001
Drank piped water at work or home	6 (11.5)	13 (20.6)	0.19
Drank bottled water at work or home	13 (25.0)	18 (28.6)	0.67
Drank river/spring water at work or home	5 (9.6)	9 (14.3)	0.45
Personal protective equipment	3 (5.8)	0 (0.0)	0.09
Exposure to any agent	32 (61.5)	10 (15.9)	<0.001
Exposure to any agent without personal protective equipment	29 (55.8)	10 (15.9)	<0.001
Exposure to paraquat	14 (26.9)	1 (1.6)	<0.001
Exposure to paraquat without personal protective equipment	14 (26.9)	1 (1.6)	<0.001
Exposure to multiple agents	7 (13.5)	3 (4.8)	0.18
Exposure to multiple agents without personal protective equipment	7 (13.5)	3 (4.8)	0.18
Exposure to unspecified agents	16 (30.8)	9 (14.3)	0.03
Exposure to unspecified agents without personal protective equipment	13 (25.0)	9 (14.3)	0.15
Exposure to other agent	8 (15.4)	2 (3.2)	0.04
Exposure to other agent without personal protective equipment	8 (15.4)	2 (3.2)	0.04
Rodent/bird	24 (46.2)	6 (9.5)	<0.001
Insect bites	35 (67.3)	16 (25.4)	<0.001

* Median (inter-quartile range) and range for continuous factors, count (percentage) for other factors

^[1]Among patients farming in original country, none of Mesoamerican nephropathy-kidney failure patient had duration of farming missing, 1 (5%) non-Mesoamerican nephropathy-kidney failure patient had duration of farming missing. Duration of farming was set to zero among patients without history of farming in original country.

^[2]Among patients exposed to any agrochemical, 2 (6.3%) Mesoamerican nephropathy-kidney failure patients had duration of exposure missing, none of non-Mesoamerican nephropathy-kidney failure patients had duration of exposure missing. Duration of period exposed to agrochemical was set to zero among patients without history of any agrochemical exposure.

^[3]Among patients exposed to any agrochemical, 6 (18.8%) Mesoamerican nephropathy-kidney failure patients had number of episodes of exposure missing, 5 (50%) of non-Mesoamerican nephropathy-kidney failure patients had episodes of exposure missing. Episodes or period of exposure to agrochemicals was set to zero among patients without history of any agrochemical exposure.

Supplemental Table 1B

Characteristics among Mesoamerican nephropathy-kidney failure patients and non-Mesoamerican nephropathy-kidney failure patients who did farm work in the original country.

Characteristic	Mesoamerican nephropathy- ESKD (N=37)	Non- Mesoamerican nephropathy- ESKD (N=20)	p-value
Age*	40.0 (34.0,46.0) 22 - 60	45.5 (39.0,54.5) 25 - 73	0.07
Age when moved to US*	23.0 (18.0,33.0) 11 - 46	25.0 (18.5,30.0) 14 - 58	0.63
US-Farming years*	0.0 (0.0,0.0) 0 - 5	0.0 (0.0,0.0) 0 - 2	0.97
US-Construction years*	0.3 (0.0,3.0) 0 - 13	1.0 (0.0,3.0) 0 - 30	0.88
US-Landscaping years*	0.0 (0.0,1.0) 0 - 12	0.0 (0.0,0.3) 0 - 3	0.45
Duration (years) farming in origin country*	9.0 (5.0,14.0)	7.0 (5.0,12.0)	0.92
^[1] [N of missing]	0.3 - 34 0	2 - 49 1	
Agrochemical exposure duration* ^[2] [N of missing]	8.0 (2.0,11.0) 0 - 23 2	0.0 (0.0,0.5) 0 - 20 0	<0.001
Agrochemical exposure episodes* ^[3] [N of missing]	45.0 (6.0,288.0) 0 - 3600 6	0.0 (0.0,2.5) 0 - 50 4	<0.001
Years in Houston*	14.0 (9.0,20.0) 1 - 30	13.0 (9.0,24.0) 3 - 43	0.6
Gender			
Female	1 (2.7)	6 (30.0)	0.003
Male	36 (97.3)	14 (70.0)	
Origin country locale			
City	5 (13.5)	2 (10.0)	0.7
Village/farm	32 (86.5)	18 (90.0)	
Highest education achieved			
Some school	33 (97.1)	13 (76.5)	0.07
High school	0 (0.0)	3 (17.6)	
College	1 (2.9)	1 (5.9)	
[N of missing]	3	3	
Literate	34 (91.9)	17 (85.0)	0.95
English - Second Language	7 (18.9)	4 (20.0)	
First degree relative with renal dx	9 (24.3)	1 (5.0)	
Diabetes mellitus	0 (0.0)	6 (30.0)	
Hypertension	0 (0.0)	12 (60.0)	0.02
Herb/alternative medication use	2 (5.4)	1 (5.0)	
Analgesic use	15 (40.5)	2 (10.0)	0.92
NSAID use	4 (10.8)	2 (10.0)	
Drug allergies	7 (18.9)	4 (20.0)	0.9
Currently employed	14 (37.8)	7 (35.0)	
US Farming	2 (5.4)	1 (5.0)	0.95
US Construction	22 (59.5)	10 (50.0)	0.5
US Landscaping	17 (45.9)	7 (35.0)	0.4

Farming in origin country	n/a	n/a	n/a
Cane Cutter	7 (18.9)	8 (40.0)	0.09
Cotton/Corn	32 (86.5)	16 (80.0)	0.5
Animals	17 (45.9)	10 (50.0)	0.8
Other produce	18 (48.6)	16 (80.0)	0.02
Lived in another U.S. city	10 (27.0)	7 (36.8)	0.45
	0	1	
Country of origin - climate hot	26 (70.3)	13 (65.0)	0.68
Hydrates while working	33 (89.2)	19 (95.0)	0.46
Drank well water at work or home	31 (83.8)	11 (55.0)	0.02
Drank piped water at work or home	3 (8.1)	3 (15.0)	0.42
Drank bottled water at work or home	3 (8.1)	1 (5.0)	0.66
Drank river/spring water at work or home	5 (13.5)	7 (35.0)	0.06
Personal protective equipment	1 (2.7)	0 (0.0)	0.46
Exposure to any agent	30 (81.1)	9 (45.0)	0.005
Exposure to any agent without personal protective equipment	29 (78.4)	9 (45.0)	0.01
Exposure to paraquat	14 (37.8)	1 (5.0)	0.06
Exposure to paraquat without personal protective equipment	14 (37.8)	1 (5.0)	0.06
Exposure to multiple agents	7 (18.9)	3 (15.0)	0.7
Exposure to multiple agents without personal protective equipment	7 (18.9)	3 (15.0)	0.7
Exposure to unspecified agents	14 (37.8)	8 (40.0)	0.87
Exposure to unspecified agents without personal protective equipment	13 (35.1)	8 (40.0)	0.7
Exposure to other agent	8 (21.6)	2 (10.0)	0.27
Exposure to other agent without personal protective equipment	8 (21.6)	2 (10.0)	0.27
Rodent/bird	21 (56.8)	3 (15.0)	0.002
Insect bites	28 (75.7)	8 (40.0)	0.008

Supplemental Table 2.

Odds ratios from crude model and model adjusting for age and sex.

Characteristic	Crude model		Model adjusting for age and sex*	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age contribution, 1 year	0.94 (0.91, 0.98)	0.001	0.94 (0.91, 0.98)	0.007
Contribution of age when moved to US, 1 year	0.98 (0.95, 1.02)	0.26	1.04 (0.98, 1.10)	0.15
Contribution of Farming while in US, 1 year	1.11 (0.63, 1.98)	0.71	0.89 (0.49, 1.59)	0.68
Contribution of Construction work while in US, 1 year	0.97 (0.91, 1.04)	0.46	0.92 (0.84, 1.00)	0.06
Contribution of Landscaping work while in US, 1 year	1.13 (0.96, 1.33)	0.14	1.03 (0.87, 1.20)	0.76
Duration (years) farming in origin country, 1 year*	1.06 (1.00, 1.11)	0.04	1.08 (1.02, 1.15)	0.01
agrochemical exposure, 1 year*	1.39 (1.18, 1.64)	<0.001	1.33 (1.12, 1.58)	0.001
Years in Houston, 1 year	0.93 (0.89, 0.98)	0.006	0.97 (0.91, 1.03)	0.26
Gender, men vs. women	21.32 (4.77, 95.30)	<.0001	20.22 (4.40, 93.05)	<.0001
Origin country locale, village/farm vs. city	1.48 (0.68, 3.21)	0.32	2.42 (0.96, 6.10)	0.06
High school/College vs. some school*	0.45 (0.20, 1.06)		0.30 (0.11, 0.83)	
Literate, Yes vs. No	1.72 (0.41, 7.24)		0.92 (0.16, 5.19)	
ESL, Yes vs. No	1.69 (0.76, 3.77)		1.02 (0.40, 2.60)	
First degree relative with renal dx, Y vs. N	1.61 (0.61, 4.25)	0.34	2.21 (0.65, 7.48)	0.2
Diabetes mellitus, Yes vs. No	n/a	n/a	n/a	n/a
Hypertension, Yes vs. No	n/a	n/a	n/a	n/a
Herb/alternative medication use, Y vs. N	5.17 (0.56, 47.73)	0.15	1.76 (0.18, 17.38)	0.63
Analgesic use, Yes vs. No	1.84 (0.82, 4.14)	0.14	1.70 (0.65, 4.41)	0.28
NSAID use, Yes vs. No	0.64 (0.29, 2.77)	0.45	0.60 (0.16, 2.26)	0.45
Drug allergies, Yes vs. No	0.81 (0.35, 1.90)	0.63	1.63 (0.55, 4.77)	0.37
Currently employed, Yes vs. No	1.83 (0.84, 3.98)		0.89 (0.35, 2.22)	
Farming while in US, Yes vs. No	1.67 (0.36, 7.81)	0.52	1.38 (0.24, 7.85)	0.72
Construction work while in US, Yes vs. No	2.22 (1.05, 4.69)	0.037	0.55 (0.21, 1.48)	0.24
Landscaping work while in US, Yes vs. No	2.95 (1.25, 6.96)	0.013	1.13 (0.43, 2.96)	0.8
Farming in origin country, Yes vs. No	5.30 (2.38, 11.81)	<0.001	4.49 (1.73, 11.62)	<0.002
Cane Cutter, Yes vs. No	1.07 (0.36, 3.18)	0.90	0.45 (0.14, 1.43)	0.18
Cotton/Corn, Yes vs. No	4.33 (1.97, 9.52)	<0.001	5.29 (1.96, 14.25)	0.001

Characteristic	Crude model		Model adjusting for age and sex*	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Animals, Yes vs. No	2.57 (1.06, 6.27)	0.04	2.00 (0.70, 5.66)	0.19
Other produce, Yes vs. No	1.56 (0.72, 3.41)	0.26	1.58 (0.61, 4.07)	0.34
Lived in another U.S. city, Yes vs. No	1.04 (0.46, 2.32)	0.93	0.86 (0.33, 2.22)	0.75
Country of origin - climate hot, Yes vs. No	1.62 (0.74, 3.55)	0.23	1.19 (0.46, 3.03)	0.72
Hydrates while working, Yes vs. No	1.62 (0.56, 4.73)	0.38	0.39 (0.08, 1.82)	0.23
Drank well water at work or home, Yes vs. No	4.70 (2.13, 10.38)	<0.001	5.08 (1.91, 13.53)	<0.001
Drank piped water at work or home, Yes vs. No	0.50 (0.18, 1.43)	0.2	0.68 (0.20, 2.30)	0.54
Drank bottled water at work or home, Yes vs. No	0.83 (0.36, 1.92)	0.67	0.48 (0.16, 1.38)	0.17
Drank river/spring water at work or home, Yes vs. No	0.64 (0.20, 2.04)	0.45	0.70 (0.18, 2.74)	0.61
Personal protective equipment, Yes vs. No	n/a	n/a	n/a	n/a
Exposure to any agent, Yes vs. No	8.48 (3.53, 20.38)	<0.001	4.86 (1.82, 12.96)	0.002
Exposure to any agent (adjusted for personal protective equipment) , Yes vs. No	6.68 (2.80, 15.94)	<0.001	3.99 (1.50, 10.62)	0.006
Exposure to paraquat, Yes vs. No	22.84 (2.89, 180.68)	<0.001	12.25 (1.51, 99.36)	0.02
Exposure to paraquat (adjusted for personal protective equipment) , Yes vs. No	22.84 (2.89, 180.68)	<0.001	12.25 (1.51, 99.36)	0.02
Exposure to multiple agents, Yes vs. No	3.11 (0.76, 12.70)	0.11	1.69 (0.39, 7.35)	0.48
Exposure to multiple agents (adjusted for personal protective equipment) , Yes vs. No	3.11 (0.76, 12.70)	0.11	1.69 (0.39, 7.35)	0.48
Exposure to unspecified agents, Yes vs. No	2.67 (1.06, 6.69)	0.04	1.55 (0.56, 4.34)	0.4
Exposure to unspecified agents (adjusted for personal protective equipment) , Yes vs. No	2.00 (0.78, 5.14)	0.15	1.23 (0.43, 3.55)	0.70
Exposure to other agent, Yes vs. No	5.55 (1.12, 27.39)	0.036	3.21 (0.61, 16.80)	0.17
Exposure to other agent (adjusted for personal protective equipment) , Yes vs. No	5.55 (1.12, 27.39)	0.036	3.21 (0.61, 16.80)	0.17
Rodent/bird, Yes vs. No	8.14 (2.99, 22.19)	<0.001	8.52 (2.51, 28.93)	<0.001
Insect bites, Yes vs. No	6.05 (2.69, 13.61)	<0.001	4.09 (1.62, 10.34)	0.003

*ORs for age and sex were from the model adjusting each other. ORs for other covariates were from the model adjusting for age and sex.

Supplemental Table 2B.

Odds ratios from crude model and model adjusting for age and sex among farm workers in original country.

	Crude model		Model adjusting for age and sex*	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age contribution, 1 year	0.95 (0.90, 1.00)	0.05	0.96 (0.91, 1.01)	0.15
Contribution of age when moved to US, 1 year	0.98 (0.93, 1.03)	0.37	1.01 (0.94, 1.09)	0.74
Contribution of Farming while in US, 1 year	1.10 (0.47, 2.53)	0.83	0.99 (0.43, 2.29)	0.97
Contribution of Construction work while in US, 1 year	0.95 (0.86, 1.05)	0.28	0.93 (0.83, 1.05)	0.25
Contribution of Landscaping work while in US, 1 year	1.31 (0.92, 1.86)	0.14	1.17 (0.85, 1.62)	0.33
Duration (years) farming in origin country, 1 year*	0.99 (0.93, 1.05)	0.64	1.02 (0.94, 1.11)	0.62
agrochemical exposure, 1 year*	1.30 (1.08, 1.55)	0.005	1.25 (1.04, 1.50)	0.02
Years in Houston, 1 year	0.97 (0.91, 1.03)	0.34	1.01 (0.94, 1.10)	0.75
Gender, men vs. women	15.43 (1.70, 139.96)	0.02	11.98 (1.28, 112.01)	0.03
Origin country locale, village/farm vs. city	0.71 (0.13, 4.05)	0.7	1.50 (0.23, 9.71)	0.7
High school/College vs. some school*	0.35 (0.07, 1.77)		0.33 (0.06, 1.85)	
Literate, Yes vs. No	2.00 (0.36, 10.98)		1.27 (0.17, 9.55)	
ESL, Yes vs. No	0.93 (0.24, 3.67)		0.64 (0.15, 2.76)	
First degree relative with renal dx, Y vs. N	6.11 (0.71, 52.25)	0.10	11.68 (0.81, 167.98)	0.1
Diabetes mellitus, Yes vs. No	n/a	n/a	n/a	n/a
Hypertension, Yes vs. No	n/a	n/a	n/a	n/a
Herb/alternative medication use, Yes vs. No	6.14 (1.24, 30.44)	0.03	5.46 (0.96, 30.99)	0.06
Analgesic use, Yes vs. No	1.09 (0.09, 12.77)	0.95	0.48 (0.04, 6.39)	0.58
NSAID use, Yes vs. No	1.41 (0.25, 8.00)	0.92	1.60 (0.23, 11.04)	0.78
Drug allergies, Yes vs. No	0.93 (0.24, 3.67)	0.92	2.13 (0.37, 12.25)	0.4
Currently employed, Yes vs. No	1.13 (0.36, 3.51)		0.61 (0.16, 2.28)	
Farming while in US, Yes vs. No	1.09 (0.09, 12.77)	0.95	0.86 (0.07, 10.52)	0.91
Construction work while in US, Yes vs. No	1.47 (0.49, 4.38)	0.49	0.79 (0.22, 2.87)	0.72
Landscaping work while in US, Yes vs. No	1.58 (0.51, 4.86)	0.43	0.69 (0.18, 2.57)	0.58
Farming in origin country, Yes vs. No	n/a	n/a	n/a	n/a
Cane Cutter, Yes vs. No	0.35 (0.10, 1.18)	0.09	0.13 (0.03, 0.57)	0.007
Cotton/Corn, Yes vs. No	1.60 (0.38, 6.79)	0.52	3.17 (0.65, 15.49)	0.15
Animals, Yes vs. No	0.85 (0.29, 2.53)	0.77	0.60 (0.16, 2.23)	0.44

	Crude model		Model adjusting for age and sex*	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Other produce, Yes vs. No	0.24 (0.07, 0.84)	0.03	0.32 (0.08, 1.23)	0.10
Lived in another U.S. city, Yes vs. No	0.63 (0.19, 2.07)	0.45	0.41 (0.11, 1.52)	0.18
Country of origin - climate hot, Yes vs. No	1.27 (0.40, 4.05)	0.68	0.63 (0.14, 2.74)	0.54
Hydrates while working, Yes vs. No	0.43 (0.05, 4.17)	0.47	0.17 (0.01, 2.73)	0.21
Drank well water at work or home, Yes vs. No	4.23 (1.22, 14.62)	0.02	5.40 (1.24, 23.59)	0.03
Drank piped water at work or home, Yes vs. No	0.50 (0.09, 2.74)	0.43	0.68 (0.09, 5.22)	0.71
Drank bottled water at work or home, Yes vs. No	1.68 (0.16, 17.25)	0.66	0.83 (0.07, 9.50)	0.88
Drank river/spring water at work or home, Yes vs. No	0.29 (0.08, 1.08)	0.07	0.35 (0.07, 1.63)	0.18
Personal protective equipment, Yes vs. No	n/a	n/a	n/a	n/a
Exposure to any agent, Yes vs. No	5.24 (1.57, 17.48)	0.007	2.64 (0.62, 11.25)	0.19
Exposure to any agent (adjusted for personal protective equipment) , Yes vs. No	4.43 (1.36, 14.40)	0.01	2.17 (0.53, 8.93)	0.28
Exposure to paraquat, Yes vs. No	11.56 (1.39, 96.12)	0.02	7.70 (0.90, 66.22)	0.06
Exposure to paraquat (adjusted for personal protective equipment) , Yes vs. No	11.56 (1.39, 96.12)	0.02	7.70 (0.90, 66.22)	0.06
Exposure to multiple agents, Yes vs. No	1.32 (0.30, 5.79)	0.71	0.85 (0.18, 3.97)	0.83
Exposure to multiple agents (adjusted for personal protective equipment) , Yes vs. No	1.32 (0.30, 5.79)	0.71	0.85 (0.18, 3.97)	0.83
Exposure to unspecified agents, Yes vs. No	0.91 (0.30, 2.78)	0.87	0.49 (0.14, 1.75)	0.27
Exposure to unspecified agents (adjusted for personal protective equipment) , Yes vs. No	0.81 (0.26, 2.49)	0.72	0.43 (0.12, 1.56)	0.20
Exposure to other agent, Yes vs. No	2.48 (0.47, 13.02)	0.28	1.69 (0.31, 9.35)	0.55
Exposure to other agent (adjusted for personal protective equipment) , Yes vs. No	2.48 (0.47, 13.02)	0.28	1.69 (0.31, 9.35)	0.55
Rodent/bird, Yes vs. No	7.44 (1.85, 29.83)	0.005	5.05 (1.17, 21.75)	0.03
Insect bites, Yes vs. No	4.67 (1.45, 15.01)	0.01	3.12 (0.85, 11.41)	0.09

Supplemental Table 3A. Odds ratios from logistic regression models characterizing relationship between agrochemical exposure and kidney failure from Mesoamerican nephropathy.

Agrochemical exposure	Model 1		Model 2		Model 3a		Model 3b		Model 3c	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Agrochemical exposure years, 1 year	1.39 (1.18, 1.64)	<0.001	1.33 (1.12, 1.58)	0.001	1.23 (1.04, 1.44)	0.02	1.26 (1.04, 1.52)	0.02	1.25 (1.04, 1.49)	0.015
Exposure to any agent, Yes vs. No	8.48 (3.53, 20.38)	<0.001	4.86 (1.82, 12.96)	0.002	1.60 (0.47, 5.46)	0.45	2.07 (0.53, 8.03)	0.3	1.25 (0.29, 5.36)	0.76
Exposure to any agent without personal protective equipment, Yes vs. No	6.68 (2.80, 15.94)	<0.001	3.99 (1.50, 10.62)	0.006	1.11 (0.31, 3.92)	0.87	1.15 (0.24, 5.55)	0.9	0.54 (0.09, 3.11)	0.5
Exposure to paraquat, Yes vs. No	22.84 (2.89, 180.68)	0.003	12.25 (1.51, 99.36)	0.02	4.14 (0.43, 39.46)	0.22	4.78 (0.52, 43.83)	0.17	4.92 (0.53, 45.25)	0.16
Exposure to paraquat without personal protective equipment, Yes vs. No	22.84 (2.89, 180.68)	0.003	12.25 (1.51, 99.36)	0.02	4.14 (0.43, 39.46)	0.22	4.78 (0.52, 43.83)	0.17	4.92 (0.53, 45.25)	0.16
Exposure to multiple agents, Yes vs. No	3.11 (0.76, 12.70)	0.11	1.69 (0.39, 7.35)	0.5	0.35 (0.06, 2.23)	0.27	0.71 (0.13, 3.76)	0.69	0.39 (0.06, 2.37)	0.3
Exposure to multiple agents without personal protective equipment, Yes vs. No	3.11 (0.76, 12.70)	0.11	1.69 (0.39, 7.35)	0.5	0.35 (0.06, 2.23)	0.27	0.71 (0.13, 3.76)	0.69	0.39 (0.06, 2.37)	0.3
Exposure to unspecified agents, Yes vs. No	2.67 (1.06, 6.69)	0.04	1.55 (0.56, 4.34)	0.4	0.78 (0.24, 2.52)	0.68	0.76 (0.22, 2.65)	0.67	0.43 (0.11, 1.69)	0.2
Exposure to unspecified agents without personal protective equipment, Yes vs. No	2.00 (0.78, 5.14)	0.15	1.23 (0.43, 3.55)	0.7	0.53 (0.15, 1.84)	0.32	0.33 (0.07, 1.53)	0.16	0.15 (0.03, 0.84)	0.03
Exposure to other agent, Yes vs. No	5.55 (1.12, 27.39)	0.04	3.21 (0.61, 16.80)	0.17	0.91 (0.13, 6.31)	0.9	1.57 (0.26, 9.66)	0.62	0.97 (0.14, 6.47)	0.97
Exposure to other agent without personal protective equipment, Yes vs. No	5.55 (1.12, 27.39)	0.04	3.21 (0.61, 16.80)	0.17	0.91 (0.13, 6.31)	0.9	1.57 (0.26, 9.66)	0.62	0.97 (0.14, 6.47)	0.97

Model 1. Crude model.

Model 2. Model adjusting for age and sex.

Model 3a. Model adjusting for age, sex, rodent/bird, and drinking well water.

Model 3b. Model adjusting for age, sex, drinking well water, and cotton/corn.

Model 3c. Model adjusting for age, sex, rodent/bird, and cotton/corn.

Supplemental Table 3B. Non-agrochemical covariates with Mesoamerican nephropathy-kidney failure showing odds ratios from model adjusted for agrochemical exposure duration.

Covariate	Model 3a		Model 3b		Model 3c	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Agrochemical exposure years, 1 year	1.23 (1.04, 1.44)	0.01	1.26 (1.04, 1.52)	0.017	1.25 (1.04, 1.49)	0.015
Age, 1 year	0.93 (0.88, 0.98)	0.008	0.93 (0.88, 0.98)	0.004	0.93 (0.89, 0.98)	0.009
Gender, men vs. women	11.73 (2.13, 64.63)	0.005	9.60 (1.97, 46.82)	0.006	13.11 (2.31, 74.42)	0.004
Rodent/bird, Yes vs. No	4.81 (1.27, 18.29)	0.022	n/a	n/a	5.06 (1.31, 19.53)	0.019
Drank well water at work or home	1.78 (0.54, 5.87)	0.34	2.00 (0.60, 6.70)	0.26	n/a	n/a
Cotton/Corn	n/a	n/a	1.31 (0.35, 4.83)	0.68	1.18 (0.31, 4.50)	0.8

Supplemental Table 4

Characteristics among Mesoamerican nephropathy-kidney failure patients and matched healthy controls.

Characteristics	value	Mesoamerican nephropathy- kidney failure (N=16)	Matched controls (N=16)
Age	median(interquartile range) range	37.5 (34.0,45.5) 26 - 60	39.0 (33.0,44.5) 24 - 57
Age when moved to US	median(interquartile range) [N of missing] range	22.5 (16.5,30.5) 0 8 - 37	25.0 (18.0,28.0) 1 13 - 37
US-Farming years	median(interquartile range) range	0 (0,0) 0 - 0	0 (0,0) 0 - 11
US-Construction years	median(interquartile range) range	0.1 (0.0,2.5) 0 - 10	0.0 (0.0,2.5) 0 - 24
US-Landscaping years	median(interquartile range) range	0.0 (0.0,3.5) 0 - 8	0.0 (0.0,0.0) 0 - 10
Duration (years) farming in origin country	median(interquartile range) range	9.0 (2.5,13.0) 0 - 28	7.5 (4.5,16.0) 0 - 20
Agrochemical exposure duration	median(interquartile range) range	6.5 (0.0,11.0) 0 - 23	1.4 (0.0,10.0) 0 - 20
Agrochemical exposure episodes	median(interquartile range) range	13.0 (0.0,172.0) 0 - 936	3.8 (0.0,45.5) 0 - 624
Elevation (m)	median(interquartile range) range [N of missing]	171.0 (102.0,1713.5) 0 - 2075 0	180.5 (116.0,1867.0) 0 - 2075 4
Years in Houston	median(interquartile range) range	12.0 (9.0,19.0) 5 - 30	10.0 (3.5,20.0) 0 - 30
Gender	Male	16 (100.0)	16 (100.0)
Origin country locale	City Village/farm	3 (18.8) 13 (81.3)	1 (6.3) 15 (93.8)
Highest education achieved	Some school High school College [N of missing]	14 (93.3) 1 (6.7) 0 (0.0) 1	9 (56.3) 5 (31.3) 2 (12.5) 0
High school/College	No Yes [N of missing]	14 (93.3) 1 (6.7) 1	9 (56.3) 7 (43.8) 0
Literate	No Yes	1 (6.3) 15 (93.8)	1 (6.3) 15 (93.8)
English as Second Language	No Yes	12 (75.0) 4 (25.0)	10 (62.5) 6 (37.5)
First degree relative with renal dx	No Yes	12 (75.0) 4 (25.0)	7 (43.8) 9 (56.3)
Diabetes mellitus	No Yes	16 (100.0) 0 (0.0)	15 (93.8) 1 (6.3)
Hypertension	No Yes	16 (100.0) 0 (0.0)	14 (87.5) 2 (12.5)
Herb/alternative medication use	No Yes	14 (87.5) 2 (12.5)	15 (93.8) 1 (6.3)

Characteristics	value	Mesoamerican nephropathy- kidney failure (N=16)	Matched controls (N=16)
Analgesic use	No	7 (43.8)	14 (87.5)
	Yes	9 (56.3)	2 (12.5)
NSAID use	No	12 (75.0)	15 (93.8)
	Yes	4 (25.0)	1 (6.3)
Drug allergies	No	14 (87.5)	15 (93.8)
	Yes	2 (12.5)	1 (6.3)
Currently employed	No	9 (56.3)	1 (6.3)
	Yes	7 (43.8)	15 (93.8)
US Farming	No	16 (100.0)	14 (87.5)
	Yes	0 (0.0)	2 (12.5)
US Construction	No	7 (43.8)	9 (56.3)
	Yes	9 (56.3)	7 (43.8)
US Landscaping	No	9 (56.3)	13 (81.3)
	Yes	7 (43.8)	3 (18.8)
Farming in origin country	No	1 (6.3)	1 (6.3)
	Yes	15 (93.8)	15 (93.8)
Cane Cutter	No	12 (75.0)	13 (81.3)
	Yes	4 (25.0)	3 (18.8)
Cotton	No	13 (81.3)	15 (93.8)
	Yes	3 (18.8)	1 (6.3)
Corn	No	3 (18.8)	2 (12.5)
	Yes	13 (81.3)	14 (87.5)
Animals	No	6 (37.5)	7 (43.8)
	Yes	10 (62.5)	9 (56.3)
Other produce	No	9 (56.3)	6 (37.5)
	Yes	7 (43.8)	10 (62.5)
Lived in another U.S. city	No	13 (81.3)	0 (0.0)
	Yes	3 (18.8)	16 (100.0)
Country of origin - climate hot	No	2 (12.5)	1 (6.3)
	Yes	14 (87.5)	15 (93.8)
Hydrates while working	No	3 (18.8)	0 (0.0)
	Yes	13 (81.3)	16 (100.0)
Drank well water at work or home	No	2 (12.5)	2 (12.5)
	Yes	14 (87.5)	14 (87.5)
Drank piped water at work or home	No	16 (100.0)	15 (93.8)
	Yes	0 (0.0)	1 (6.3)
Drank bottled water at work or home	No	14 (87.5)	14 (87.5)
	Yes	2 (12.5)	2 (12.5)
Drank river/spring water at work or home	No	13 (81.3)	14 (87.5)
	Yes	3 (18.8)	2 (12.5)
Personal protective equipment	No	16 (100.0)	8 (50.0)
	Yes	0 (0.0)	8 (50.0)
Exposure to any agent	No	4 (25.0)	7 (43.8)
	Yes	12 (75.0)	9 (56.3)
Exposure to any agent (adjusted for personal protective equipment)	No	4 (25.0)	15 (93.8)
	Yes	12 (75.0)	1 (6.3)
Exposure to paraquat	No	7 (43.8)	9 (56.3)

		Mesoamerican nephropathy- kidney failure (N=16)	Matched controls (N=16)
Characteristics	value		
	Yes	9 (56.3)	7 (43.8)
Exposure to paraquat	No	7 (43.8)	15 (93.8)
(adjusted for personal protective equipment)	Yes	9 (56.3)	1 (6.3)
Exposure to multiple agents	No	12 (75.0)	10 (62.5)
	Yes	4 (25.0)	6 (37.5)
Exposure to multiple agents (adjusted for personal protective equipment)	No	12 (75.0)	16 (100.0)
	Yes	4 (25.0)	0 (0.0)
Exposure to unspecified agents	No	13 (81.3)	15 (93.8)
	Yes	3 (18.8)	1 (6.3)
Exposure to unspecified agents (adjusted for personal protective equipment)	No	13 (81.3)	16 (100.0)
	Yes	3 (18.8)	0 (0.0)
Exposure to other agent	No	12 (75.0)	10 (62.5)
	Yes	4 (25.0)	6 (37.5)
Exposure to other agent (adjusted for personal protective equipment)	No	12 (75.0)	16 (100.0)
	Yes	4 (25.0)	0 (0.0)
Rodent/bird	No	6 (37.5)	5 (31.3)
	Yes	10 (62.5)	11 (68.8)
Insect bites	No	4 (25.0)	5 (31.3)
	Yes	12 (75.0)	11 (68.8)

Supplemental Table 5

Differences of continuous characteristics between Mesoamerican nephropathy-kidney failure and healthy controls in matched pairs.

Characteristics	(N=16)	Range	P-value from Wilcoxon signed rank test
	Median (Inter-quartile range)		
Age	1.5 (-4.0, 4.5)	-19 , 10	0.7
Age when moved to US	0.0 (-8.0, 6.0)	-20 , 17	0.9
US-Farming years	0.0 (0.0, 0.0)	-11 , 0	0.5
US-Construction years	0.0 (-1.0, 2.5)	-24 , 8	0.53
US-Landscaping years	0.0 (0.0, 0.7)	-8 , 8	0.52
Duration (years) farming in origin country	-1.8 (-7.0, 6.0)	-18 , 22	0.72
Agrochemical exposure period	0.0 (-1.5, 10.5)	-19 , 17	0.56
Agrochemical exposure episodes	0.0 (-6.8, 74.0)	-464 , 936	0.47
Years in Houston	0.5 (-4.5, 9.5)	-8 , 11	0.17

Difference on age when moved to US was missing in one pair.

Supplemental Table 6

Matched pairs with discordant categorical characteristics among Mesoamerican nephropathy-kidney failure and matched controls.

Characteristics	Number of discordant pairs (N=16)		Exact p-value from McNemar's test
	Yes only in Mesoamerican nephropathy- kidney failure	Yes only in control	
Origin country locale in village/farm	1	3	0.63
High school/college literate	0 1	5 1	
ESL	0	2	
First degree relative with renal dx	1	6	0.13
Diabetes mellitus	0	1	
Hypertension	0	2	
Herb/alternative medication use	2	1	1
Analgesic use	9	2	0.07
NSAID use	4	1	0.4
Drug allergies use	1	0	1
Currently employed	1	9	
US Farming	0	2	0.5
US Construction	5	3	0.73
US Landscaping	4	0	0.13
Farming in origin country	1	1	1
Cane Cutter	2	1	1
Cotton	2	0	0.5
Corn	1	2	1
Animals	3	2	1
Other produce	2	5	0.5
Lived in another U.S. city	0	13	<0.001
Country of origin - climate hot	0	1	1
Hydrates while working	0	3	0.25
Drank well water at work or home	1	1	1
Drank piped water at work or home	0	1	1
Drank bottled water at work or home	1	1	1
Drank river/spring water at work or home	3	2	1
Personal protective equipment	0	8	0.008
Exposure to any agent	4	1	0.38
Exposure to any agent (adjusted for personal protective equipment)	12	1	0.001
Exposure to paraquat	3	1	0.63
Exposure to paraquat (adjusted for personal protective equipment)	9	1	0.008
Exposure to multiple agents	1	3	0.63

Characteristics	Number of discordant pairs (N=16)		Exact p-value from McNemar's test
	Yes only in Mesoamerican nephropathy- kidney failure	Yes only in control	
Exposure to multiple agents (adjusted for personal protective equipment)	4	0	0.13
Exposure to unspecified agents	3	1	0.63
Exposure to unspecified agents (adjusted for personal protective equipment)	3	0	0.25
Exposure to other agent	0	2	0.5
Exposure to other agent (adjusted for personal protective equipment)	4	0	0.13
Rodent/bird	2	3	1
Insect bites	3	2	1

Survey for Dialysis Patients

Patient MRN number _____

Demographics:

Age _____ Gender _____ Home Country _____

Years of education _____ Knows how to read: Yes/No Knows English: Yes/No

Immigration History/Motivation

At what age did you leave your home country? _____

Did you live in any other countries besides your home country and the U.S.? If yes, list countries and number of years in each country

At what age did you move to the U.S.? _____

What was your motivation for moving to the U.S? job family
other _____

How many years did you live in the U.S. before initiating dialysis? _____

What was your age when you began dialysis? _____

How many years have you been in Houston (round to nearest year)? _____

What was your motivation for moving to Houston? job family
other _____

Have you lived in another city in the USA besides Houston? Yes No

If yes, which ones and for how long (nearest number of years):

Motivation for living in that city? job family other

If yes, how many? _____

Were those friends living in the United States or home country when they developed kidney disease?

United States

Home Country

Other

Name of hospital/facility where you receive dialysis most frequently? _____

Name of hospitals/facilities where you receive dialysis sporadically both in the United States and abroad? _____

General Health:

Known diseases:

Known diseases prior to dialysis:

Medication use prior to dialysis? (ask specifically about diabetes treatments, hypertension treatments, herbs/alternative medicines and pain medication use, include names if possible)

Known drug allergies:

Work History

Do you currently work? Yes No

If yes, what type of work? _____

For how long? _____

If, no how much time since you have stopped working?

Reason for stopping work _____

Who is supporting you? Family Other

Types of job in the US:

Farming Yes, Number of years No

Construction/Painting (years) Yes, Number of years No

Landscaping Yes, Number of years No

Other Yes, Number of years No

Below please list each job and number of years

Types of jobs before coming to US and duration:

Farming Yes, Number of years____No
In which country

Construction/Painting (years) Yes, Number of years____No
In which country

Landscaping Yes, Number of years____No
In which country

Other Yes, Number of years____No
In which country

Below please list each job and number of years

Have you worked in agriculture? Yes No

Number of years? _____

If yes, what type: Cane cutter Cotton farm Corn farm

 Animal farmer Other

: _____

Possible Exposures:

Rodents and birds Yes No

Insect bites Yes No

Pesticides, Herbicides, or Chemicals: Yes No

 If yes, what are the names and how were they used (was PPE/post-washing utilized):

For how long were you exposed (number of years):

How often were you exposed (times/week, weeks/year, and number of years): _____

Are you able to hydrate while at work? Yes No

What do you most commonly drink while working? Water Soda

 Flavored Water Juice

If water, what is the source? Piped water Well River/Spring

 Bottled Water Other

What type of food did you eat while working? If includes fruits, vegetables, or locally produced grains, where was the food collected? Was it near farmland? Is this food different than the food that other family members consume? Is this the same food that you eat at home?

Living Conditions:

Living location in native country:	City	Village/Farm
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Home country climate:	Hot	Cool
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Home country living location:	Close to Ocean Valley	Mountains Other
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Drinking water source at home:	Piped water Bottled Water	Well Other	River/Spring
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What type of food did you eat while at home? If includes fruits, vegetables, or locally produced grains, where was the food collected? Was it near farmland? Is this food different than the food that other family members consume?

Additional comments from discussion:
