

# A longitudinal evaluation of kidney function among sugarcane workers in Guatemala

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# Disclosures

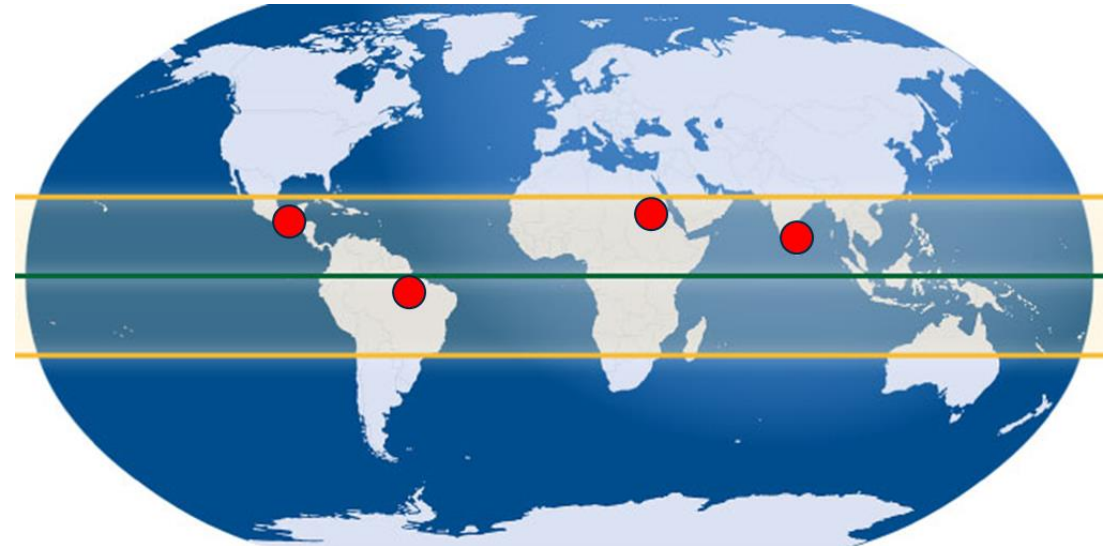
- CU MOU and contract with Pantaleon Group to apply Total Worker Health® principles to worker health, safety & well-being
- CU investigators received partial salary from contract
- Speakers have no financial or other relationship to any devices, products, laboratories or services

# Overview

1. Chronic kidney disease of unknown origin (CKDu)
2. CKDu epidemiology in Central America
3. Evaluation of sugarcane workers in Guatemala
  - Methods
  - Results
  - Summary
4. Future research

# Worldwide distribution of CKDu

- Progressive loss of kidney function
- Unknown etiology, not linked to diabetes, hypertension, or other common causes
- Clusters of CKDu
  - Past 2 decades
  - Hot / humid regions
  - Poor agricultural communities
  - Males
  - Aged 30 to 60 years
- Likely multifactorial



# Leading hypotheses for CDKu epidemic

## 1. Occupational exposures

- Repetitive dehydration
- Heat stress
- Acute kidney injury leading to CKDu

## 2. Environmental exposures

- Nephrotoxic heavy metals in drinking water
- Agrochemicals in work or home environment (dermal, inhalation, ingestion)
- Bioaccumulation of chronic low exposures



# Other hypothesized risk factors

- Nephrotoxic agents
  - NSAIDs
  - Nutrition (highly sweetened beverage consumption)
  - Tobacco
  - Infectious diseases, e.g. Leptospirosis
- Personal risk factors
  - Acclimatization differences
  - Genetics
- Additive effects
  - Dehydration + nephrotoxins
  - Failure to excrete toxicants -> increased bioaccumulation

# Epidemiology of CKDu in Central America

- >20,000 deaths, 2005-09
- Leading cause of mortality in Nicaragua & El Salvador
- Main risk factors:
  - Lower altitude communities
  - Males
  - Occupation
    - Sugarcane: greatest prevalence
    - Cotton & mine: less frequent
    - Coffee: no excess disease



# Evaluation of sugarcane workers in Guatemala

## Objectives:

1. Describe disease epidemiology
2. Examine risk factors associated with kidney function across harvest





# Sugarcane plantation practices

- 4,000 field workers hired annually
  - Local and migrant workers
  - Cane cutters and production workers
- Pre-employment health screening
  - Past medical history survey
  - Medical examination
  - Serum creatinine < 1.45 mg/dL



# Sugarcane work

- Heavy exertion
- Long work hours (>8 hours)
- Intense heat & sun exposure
  - Heat conditions exceed OSHA recommendations
- Machetes to cut cane
- Paid by amount of cane cut (average 6 tons/day)



# Health promotion practices

- Water, rest and shade guidelines
  - $\geq 2.5$  L electrolyte solution
  - $\geq 16$  L water
  - Breaks: 3 x 30 min and 1 x 60 min
- Field nurse aides and physicians
  - Educate: hygiene, nutrition and risks of using drugs and non-prescription medicines
  - Address health issues in field
- PPE
  - Goggles, hat, gloves, wrist / shin guards, boots



# Methods

## Pre-employment screening

- N=4000
- Survey
- Medical exam
- Serum creatinine to calculate eGFR

November 2015

## End of harvest rescreening

- N=407
- Survey
- Medical exam
- Serum creatinine to calculate eGFR

May 2016

6-month harvest season



Photo courtesy of Amanda Walker

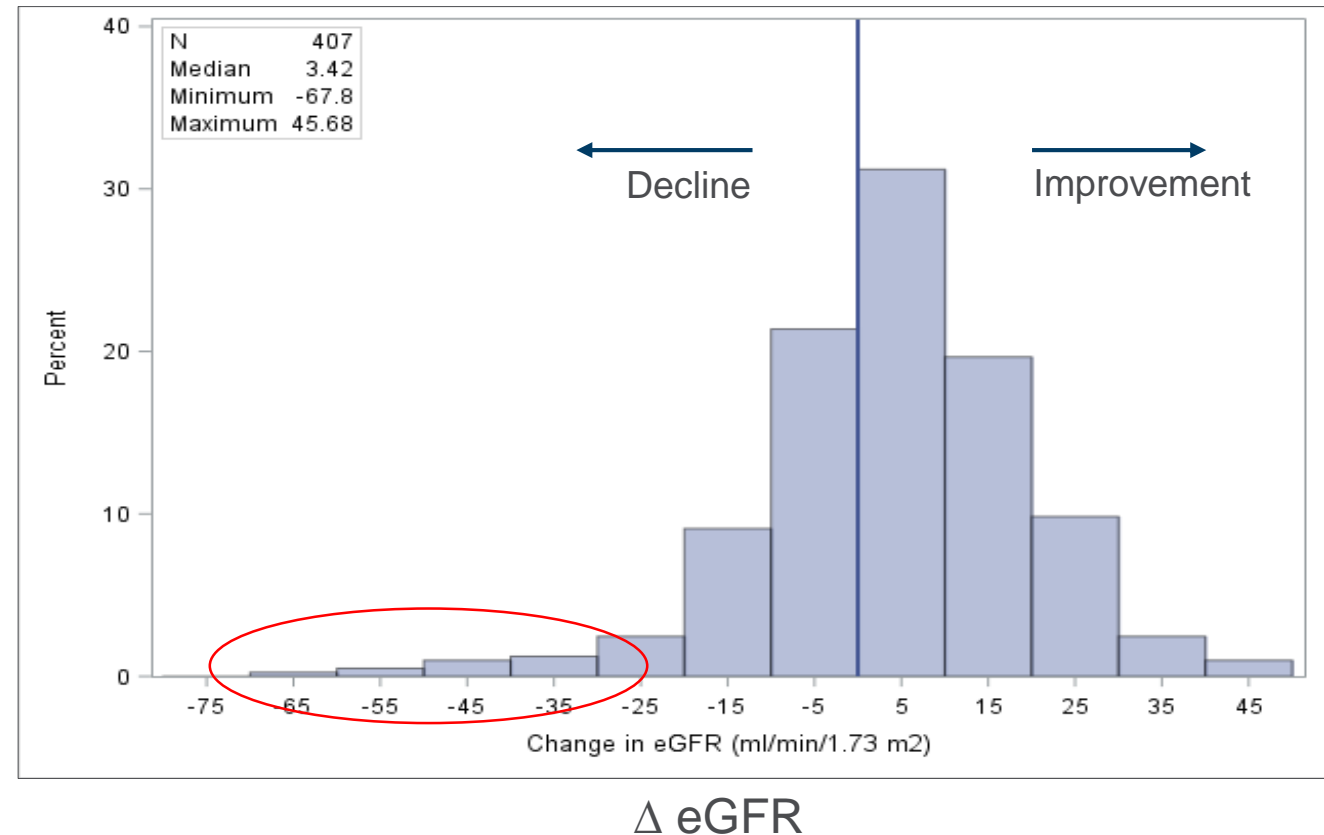
# Results: Kidney function outcomes

## Outcome 1: eGFR<60, end of harvest

- Incidence: 3% (21/407)
- 22% of 4000 workers left early
  - Worse kidney function at pre-employment
  - More likely to be from highlands

## Outcome 2: $\Delta$ eGFR

- Stable/improved: 64% (260/407)
- Decline: 36% (147/407)
  - 6% (24/407) decline eGFR>20%



# Results: Univariate risk factors of eGFR < 60

	Abnormal, eGFR < 60 n=21	Normal, eGFR ≥ 60 n=386	p-value
<b>Residence</b>			
Local	8%	92%	<b>&lt; 0.01</b>
Migrant	2%	98%	
<b>Pre-employment eGFR</b>			
Abnormal	73%	37%	<b>&lt; 0.01</b>
Normal	3%	97%	
<b>Hypertension</b>	10%	90%	0.49
<b>Diabetes</b>	0	100%	0.81
<b>Days worked</b>	141 (9)	146 (9)	<b>0.01</b>
<b>Ave tons cut/day</b>	5.3 (0.6)	5.8 (0.8)	<b>0.02</b>
<b>Water intake/day (L)</b>			
1-4	15%	85%	<b>0.04</b>
5-10	4%	96%	
> 10	4%	96%	
<b>Soda or juice glasses/day</b>			
≤ 1	4%	96%	0.17
2	6%	94%	
≥ 3	10%	90%	
<b>Tobacco smoker</b>			
Current	12%	88%	<b>&lt; 0.01</b>
Never/Former	4%	96%	
<b>NSAIDs, ≤3 months</b>			
No	2%	98%	<b>0.04</b>
Yes	7%	93%	

# Results: Multivariate risk factors of eGFR < 60

Abnormal eGFR (<60) at end of harvest*		
	Odds Ratio (95% CI)	p-value
High pre-employment creatinine, >1.25 mg/dL (ref: ≤ 1.25)	28.54 (9.68-84.18)	< 0.01
Current smoker (ref: Never/former)	2.90 (0.87-9.67)	0.08

\*Controlled for age

# Results: Multivariate risk factors of $\Delta$ eGFR

Change in eGFR during harvest*		
	Mean Difference ( $\beta$ )	p-value
<b>Worksite</b>		
A	-11.93	<b>&lt;0.01</b>
B	ref	
<b>Residence</b>		
Local	-3.67	<b>0.02</b>
Migrant	ref	
<b>Tobacco Smoker</b>		
Current	-4.90	<b>0.03</b>
Never/former	ref	

\*Controlled for age



# Summary

- Decline in kidney function related to both occupational and individual factors.
- 36% of workers had decline in kidney function, despite efforts to improve hydration, rest and shade.
  - No sig. differences between those who declined vs. improved: water intake, electrolyte solution intake, or physical exertion.
  - Drivers *in addition to* heat stress and dehydration may contribute.
- 22% of 4000 workers left early: healthy worker effect likely.
  - May have undiagnosed kidney injury.
  - May be acclimatization (migrant workers more likely to leave early).

# Future research

- Collect quantitative measurements of environmental exposures and risk factors.
  - Nephrotoxic agrochemicals and heavy metals in water sources, NSAID use, tobacco use, hydration status and heat stress
- Collect data at earlier, multiple time points during season to evaluate disease progression and reasons workers leave early.
- Evaluate interventions that aim to increase hydration, rest and include tobacco cessation.

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# Criteria of typical CKD\*

- Serum creatinine used to calculate reduced kidney function, eGFR
- One of the following criteria for > 3 months:
  1. GFR <60 mL/min per 1.73m<sup>2</sup>
    - (CKD stage 3 or worse)
  2. Marker of kidney damage found

**Table 10. Stages of Chronic Kidney Disease**

<b>Stage</b>	<b>Description</b>	<b>GFR (mL/min/1.73 m<sup>2</sup>)</b>
<b>1</b>	Kidney damage with normal or ↑ GFR	≥90
<b>2</b>	Kidney damage with mild ↓ GFR	60–89
<b>3</b>	Moderate ↓ GFR	30–59
<b>4</b>	Severe ↓ GFR	15–29
<b>5</b>	Kidney failure	<15 (or dialysis)

[http://www2.kidney.org/professionals/KDOQI/guidelines\\_ckd/p4\\_class\\_g1.htm](http://www2.kidney.org/professionals/KDOQI/guidelines_ckd/p4_class_g1.htm)

\*National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (KDOQI)

# Agribusiness Partnership

- Pantaleon – major sugar cane producer in Central America
- Goal - to assess and improve the health, safety, and well-being of its sugarcane workers in Guatemala
- Independent analysis and authority to publish findings

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Photo courtesy of Amanda Walker

# Results: Demographics

## Individual factors

- Age: 28 yrs (median), 18-67y
- Migrant: 50%
- Used pesticides on own land: 39%
- $\geq 1$  sugary drinks: 98%
- NSAID use in past 3 months: 70%
- Current smokers: 13%

## Occupational factors

- Cane cutters: 82%
- Worksite A: 76%
- Harvests worked: 8 (median)
- $>10$  L water at work per day: 74%
- Electrolyte solution per day: 2.5 L (median)