Research on the CKDnT epidemic in Central America Practical implications for decision-making

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- 30 years at IRET (Central American Institute for Studies on Toxic Substances), Universidad Nacional, Heredia Costa Rica
- Co-founder and Regional Director of SALTRA (Central American Program on Work, Environment and Health), 2003 - 2013

Severe fatal epidemic of chronic kidney disease of non traditional origin (CKDnT) in Mesoamerica

- An epidemic of chronic kidney disease in the lowlands along the Pacific coast from Mexico to Panama
- **CKDnT**: CKD of nontraditional origin, unrelated to hypertension, diabetes or obesity
- Also called Mesoamerican nephropathy in this region

Along the Pacific coast, in the lowlands

Summary of research history of Mesoamerican nephropathy

1990s **'Anecdotal' observations** by sugarcane workers and physicians in Central America:
- Sugarcane Nephropathy

2002 First publication from El Salvador:
- Trabanino et al, Rev Panam Salud Pública, 2002

2000 - **Exploratory studies** to generate hypotheses and determine extension and severity
- **Working conditions** and kidney dysfunction of **sugarcane workers**
- **Mortality** patterns by geographic areas and over time
- **Prevalence** of kidney dysfunction in distinct communities
- **Social determinants:** access to social security, subcontracting, child labor

2005 - **International research workshops** organized by SALTRA in 2005, 2009, 2012

Next workshop planned for November 2015

2012 - **In-depth studies**, further exploring and testing hypotheses

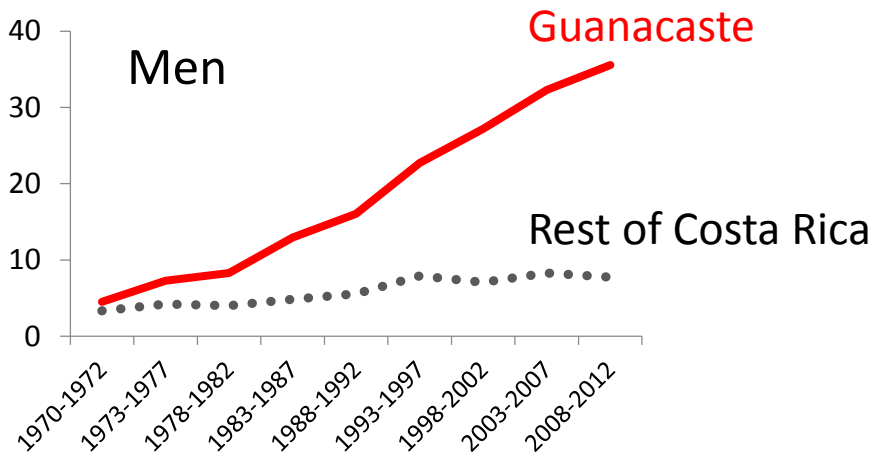
Exploratory studies: Where, who and when?

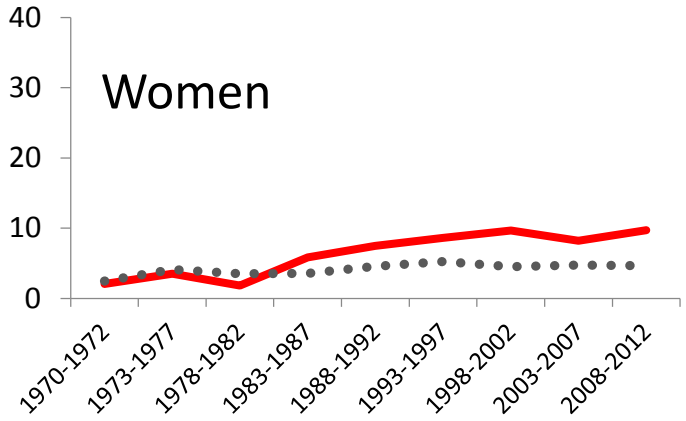
- Most Central American countries have **high CKD mortality** rates
- Large **variations** in mortality rates between regions **within countries**
- **Within affected regions**, prevalence of CKDnT **varies between communities**
- Rates much higher for **men**, but also increased among women
- CKDnT concentrates in **agricultural communities**, in particular **sugarcane workers**
- In affected areas, in lesser extent, also in **other hot occupations**
  - Construction, cotton, corn, miners, port workers
- **Young workers**, increasingly
- Increased male mortality is noticeable among men in Costa Rica **from the 1970s**

More descriptive data are needed, especially in Guatemala, Honduras, Panama, Mexico

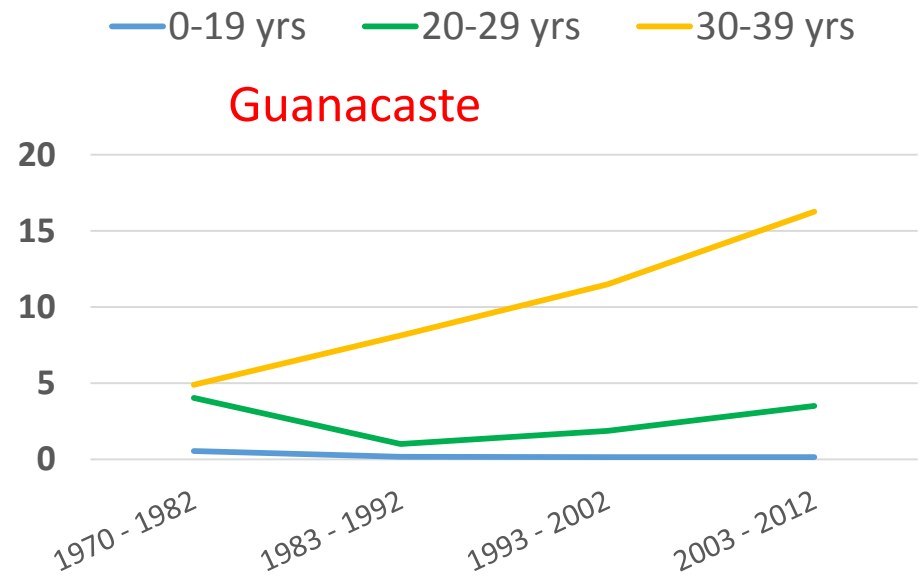
Time trends of CKD mortality in Costa Rica, 1970 - 2012

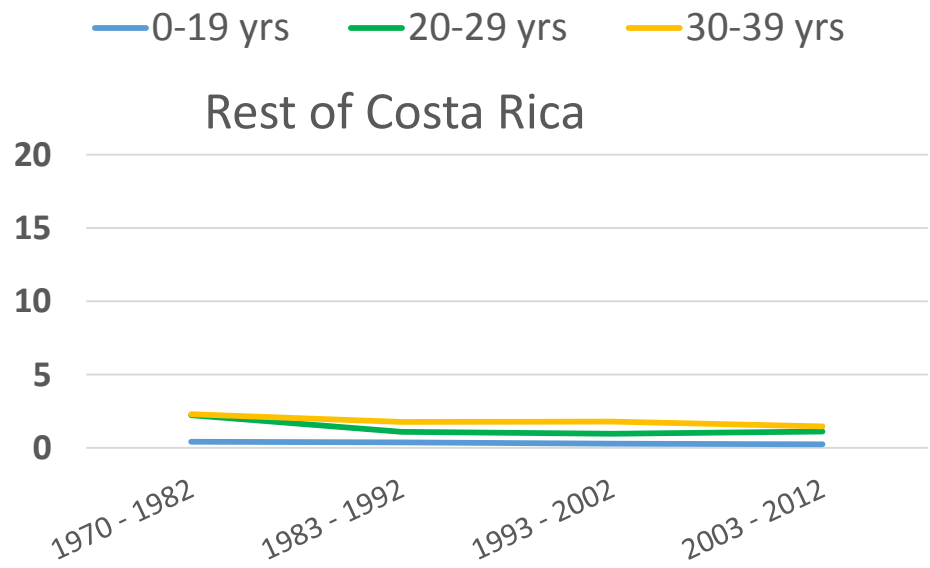
Age-adjusted rates per 100.000





Age-specific rates per 100.000





(Wesseling et al, submitted, 2014)

Main hypotheses CDKnT epidemic in Central America

Occupational exposures to **pesticides**

Environmental exposures

- Contamination of drinking water with pesticides, arsenic, cadmium
- Hard water, possibly in combination with glyphosate

Leptospirosis or other infectious agents

Behavioral exposures

- Consumption of (illegal) alcohol
- Non-steroidal anti-inflammatory drugs (NSAIDs), nephrotoxic antibiotics, diuretics
- Urinary tract infections, STDs

Genetic susceptibility

Occupational heat stress with chronic dehydration leading to repeated episodes of AKI which in turn leads to CKD

- Interaction with other environmental, behavioral or genetic risk factors

Recent in-depth research on Mesoamerican nephropathy

Sorting out emergence of CKDnT among populations at risk, Nicaragua & El Salvador:

- Follow-up studies of sugarcane workers, community members in a high risk area
- Comparison of different occupations

Mechanisms and physiopathological pathways of kidney damage in MeN

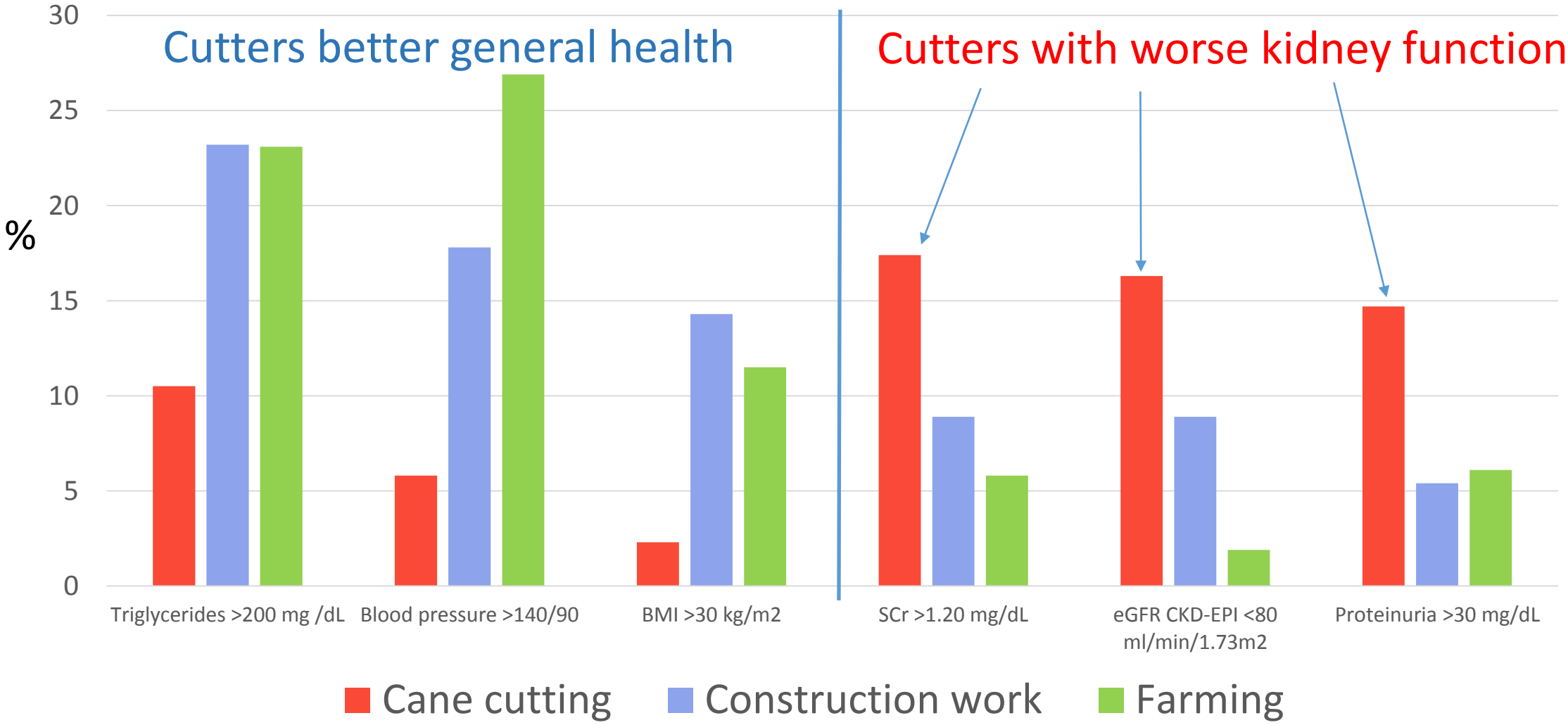
- Biopsies: El Salvador, Nicaragua, comparisons with Sri Lanka
- Pre and post shift examinations in sugarcane cutters: markers of dehydration, kidney injury and kidney dysfunction, subclinical episodes of rhabdomyolysis, uric acid metabolism
- Animal experiments: dehydration, fructose, uric acid metabolism
- Kidney damage early in life, genetic susceptibility

Access to health care, effectiveness of available treatments, socioeconomic costs and consequences: understudied

2014: Intervention study - Water Rest Shade - in sugarcane cutters in El Salvador

- Evaluation of reduction of heat stress and dehydration, and impact on kidney function
- Evaluation of production efficiency. **First results pilot phase expected in June 2015.**

Nicaraguan sugarcane cutters compared to construction workers and farmers, aged 18 - 39: León, Nicaragua, 2013.



(Wesseling et al, manuscript, 2014)

Three important studies recently published

Cohort cane cutters, one harvest, Nicaragua (McLean et al, report 2012; Laws et al, IJOEH, 2015)

- Over the harvest time, jobs with highest heat stress had the largest loss of kidney function and highest levels of markers of kidney injury
- Conclusion that the epidemic is, at least, part occupational and that the findings are consistent with repeated dehydration and heat stress during the harvest.

Cane cutters pre-shift and post-shift at end of harvest, Brazil (Paula-Santos et al, KI, 2014)

- Dehydration and decreased kidney function
- CPK tripled over the workday: marker of muscle damage from exercise which damages the kidney
- 18.5% of cane cutters had results compatible with AKI at the end of the day

Thai cohort of 40,000 workers, 2005 - 2009 (Tawatsupa et al, J Epidemiol, 2012)

- Risk for medically diagnosed CKD in 2009 was:
  - 50% higher in the group that had reported occupational heat exposure in 2005
  - Twice as high among those with prolonged heat exposure (both in 2005 and 2009)
  - Five times higher among those with prolonged heat exposure over age 35

Practical implications for decision-making

- Central American approach: COMISCA
- Surveillance
  - Full characterization of geographical extent and types of populations at risk
  - Early detection important for early treatment
- Regulatory actions to prevent occupational heat exposure and dehydration
  - Specifically for the sugarcane industry
  - Regulations for agriculture, construction, mining & any other pertinent industry or occupation
- Regulations should be based on sound and independent research
  - Commission research on open questions to qualified and acknowledged research groups, international collaborations. SALTRA and CENCAM may play a facilitating role.
- Address other likely contributing factors or disease progressing factors with common sense and precautionary principle
  - Stricter pesticide regulations and reduction of pesticide exposures
  - Agricultural policies towards alternative pest control methods
  - Address sources of exposure to arsenic drinking, water contamination
- Health services improvements, based on equity