# GAPSYM 11: HEALTH IN AFRICA - AN INTERDISCIPLINARY APPROACH
# 15 December 2017 – Ghent University

## Sub-topic 5: Childhood malnutrition in Sub-Saharan Africa

# Konzo, a toxic-nutritional neurological disease with multiple and cumulative risks in neurodevelopmental health in sub-Saharan Africa. .

Okitundu Luwa D, MD PhD1; Bumoko MB, MD PhD 1; Mayambu B MD PhD 2, Mumba N MD PhD 3,4 ; Boivin M MPH PhD 5; Tshala-Katumbay Désiré MD PhD6

**Affiliation des auteurs**
**1Departement de Neurologie, Université de Kinshasa, République Démocratique du Congo(RDC),2 Programme National de Nutrition, RDC, 3Departement de Médecine Tropicale, Université de Kinshasa & 4Institut National de Recherche Biomédicale, RDC, 5Michigan State University, MI, USA;6Department of Neurology, Oregon Health & Science University, Portland OR, USA.**
**Correspondance :**
**Okitundu Luwa E-Andjafono, Daniel, MD, PhD.**
**Unité de Neuropsychologie, Département de Neurologie**
**Centre Neuro-Psycho-Pathologique de l'Université de Kinshasa**
**Avenue des Cliniques, BP 825, Kinshasa XI**
**Téléphone : + 243999923381**
**E-mail : danielokitundu@hotmail.com/ daniel.okitundu@unikin.ac.cd**

konzo: upper –motor neuronal disease with multiple disabilities related to dietary cyanide intoxication

# Overview

Introduction

Methodological Approach

Definition of konzo

Clinical  criteria of konzo diagnosis

Epidemiological aspects of konzo

Markers of multiple and cumulative risks of neurodevelopmental health in konzo

Conclusion

# Introduction

**Documentary study  undertaken to demonstrate multiple and cumulative risks associated with konzo and the necessity of holistic approch in research and prevention of this disease.**

# Methods : Documentary study and field research experience in multidisciplinary team

Our Multidisciplinary team of field investigators

**Data Source :**

**Data basa of konzo NIH (USA)-DRC Project: Konzo papers (Tshala, 2011) et Konzo publications (Tyleskar, 2011);**

**Search motors: google scholar, pubmed, global sciences. Org;Mesh terms: cassava, cassava cyanogen neurotoxicity, konzo, spastic paraparesis**

**121 References**

# Definition of konzo

**konzo, an upper motor neuron disease, characterized by an abrupt onset of an irreversible, non-progressive, and symmetrical spastic para/Tetraparesis** (Tshala-Katumbay Désiré, et al. Neuroepidemiology of konzo − a spastic para/tetraparesis of acute onset in a new area of the Democratic Republic of Congo. African Journal of Neurological Sciences 2001, 20(1): 8-12)/

# Clinical criteria of konzo diagnosis :Konzo: WHO 1996 Criteria

1. **A visible symmetric spastic abnormality of gait while walking or running ;**
2. **A history of onset of less than 1 week followed by a non-progressive course in a formerly healthy person ;**
3. **A bilaterally exaggerated knee or ankle jerks without signs of disease of the spine.**

**WHO. Konzo, a distinct type of upper motoneuron disease. Wkly Epidemiol Rec 1996; 71 (30): 225-232.**

# Criteria of clinical diagnosis (continued) : 3 degrees of disability occasioned by konzo

1. MILD (Stade1) when the patients do not need to regularly use any walking aid ;

2. MODERATE (Stade2) when the patients are regularly using 1 or 2 stick(s) or crutches, and ;

3. SEVERE (Stade3) when the patients are bedridden or unable to walk without living support.

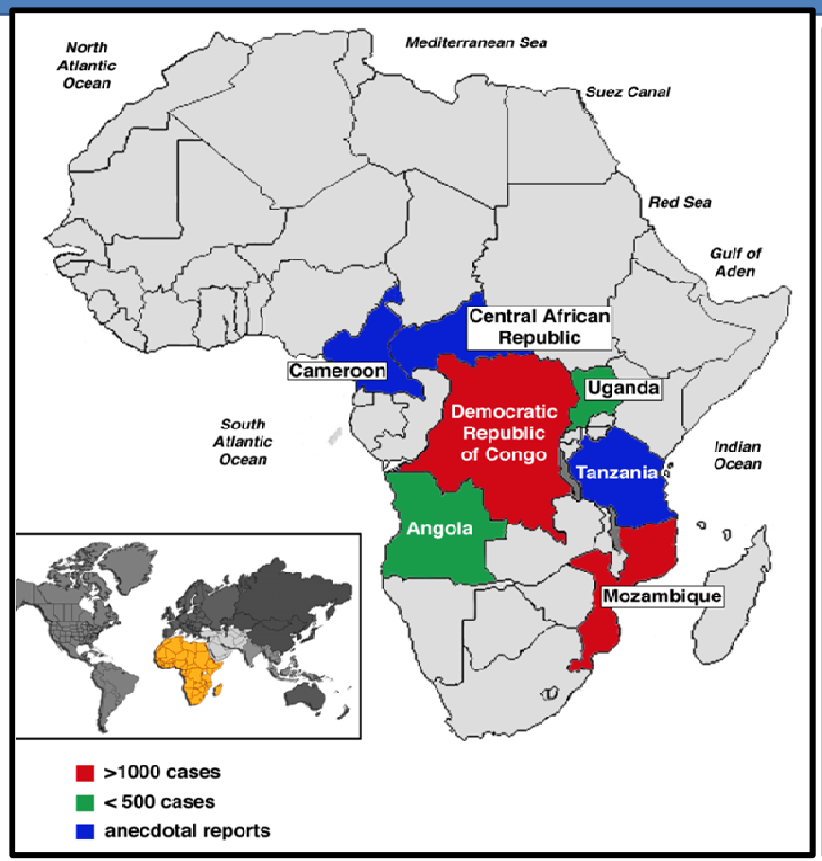
WHO. Konzo, a distinct type of upper motoneuron disease. Wkly Epidemiol Rec 1996; 71 (30): 225-232.

# Epidemiological aspects of konzo

Manihot Esculenta , main source of food for one billion of people in the world

**Konzo is a toxico-nutritional neurological disease affecting poor people in rural areas of Sub-Saharan Africa, relying on a monotonous diet based on poorly detoxified bitter cassava products in malnutrition conditions. Cassava is a source of food for nearly one billion people worldwide, from 105 countries, with 65% of consumption in Africa** (Tylleskar T, Banea M, Bikangi N, Cooke RD, Poulter NH, Rosling H. Cassava cyanogens and konzo, an upper motoneuron disease found in Africa. Lancet 1992; 339(8787): 208-11; Saunders, 2009 ; FAO Perspectives de l'alimentation : analyse des marchés mondiaux, novembre 2008 ; Agbor Egbe T., Brauman A., Griffon D., Trèche S. 1995 : Importance du manioc dans l' alimentation humaine dans différentes régions du monde. Centre DGRST-ORSTOM, Brazzaville (Congo), Editions ORSTOM, 1995).

# Epidemiological aspects of konzo (continued 1)




**According to WHO, average prevalence of konzo is 1% of the exposed population,**

**4 to 7% in some areas, particularly in the Democratic Republic of Congo (DRC).**

**Konzo-affected countries include Tanzania, Mozambique, Central African Republic, Cameroon, Angola, Uganda and recently Zambia**

Banea M, Bikangi N, Nahimana G, Nunga M, Tylleskär T, Rosling H. High prevalence of konzo associated with a food shortage crisis in the Bandundu region of zaire. Ann Soc Belg Med Trop. 1992 Dec;72(4):295-309. French. PMID: 1292426; J .P. Baneaa, J. Howard Bradburyb,⁎, C. Mandombic, D. Nahimanaa,Ian C. Dentonb, Matthew P. Fosterb, N. Kuwaa, D. Tshala Katumbayda. Konzo prevention in six villages in the DRC and the dependence of konzo prevalence on cyanide intake and malnutrition
Toxicology Reports 2 (2015): 609–616.

# Epidemiological aspects of konzo (continued 2):Contextual factors and konzo-affected subjects

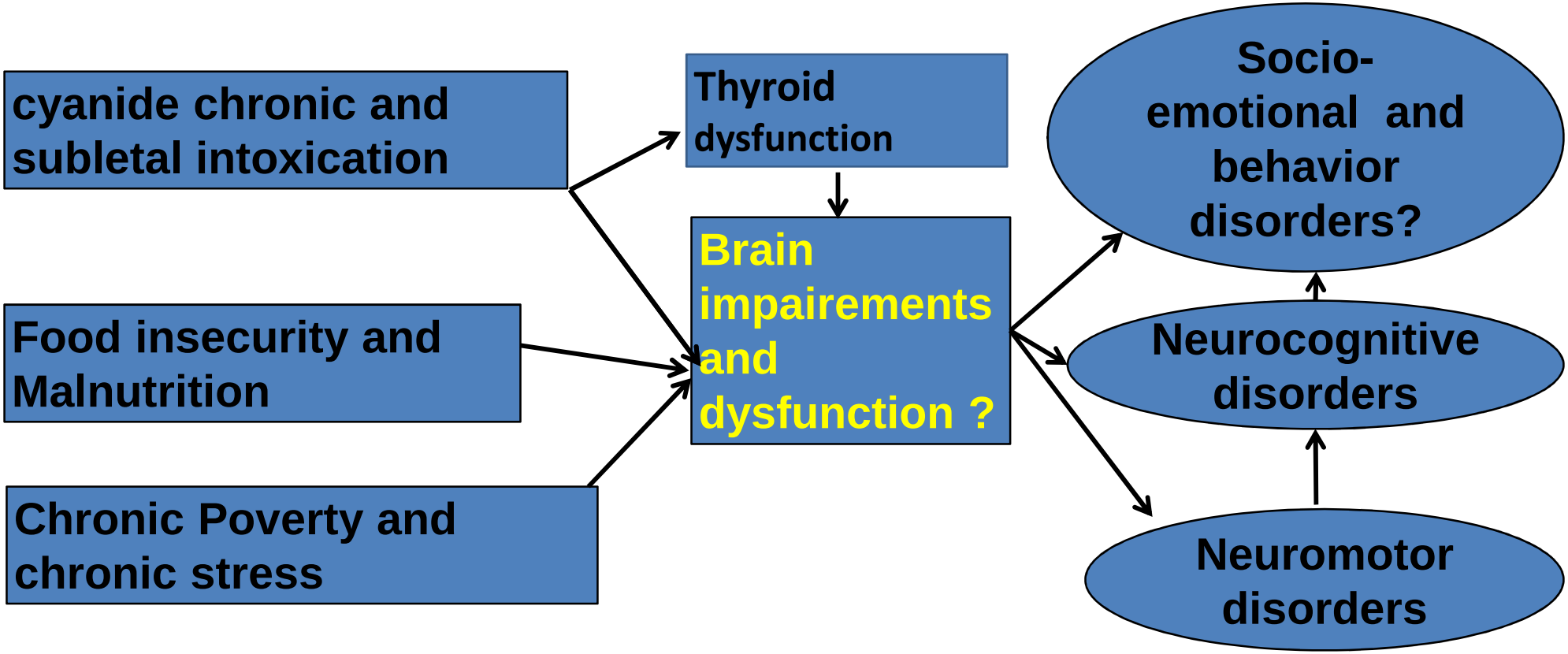
**Contextual Factors: Food insecurity, chronic malnutrition with insufficient intake of thiosulfur amino acids**

**Chronic and/or Acute stress (poverty, drought, and armed conflict).**

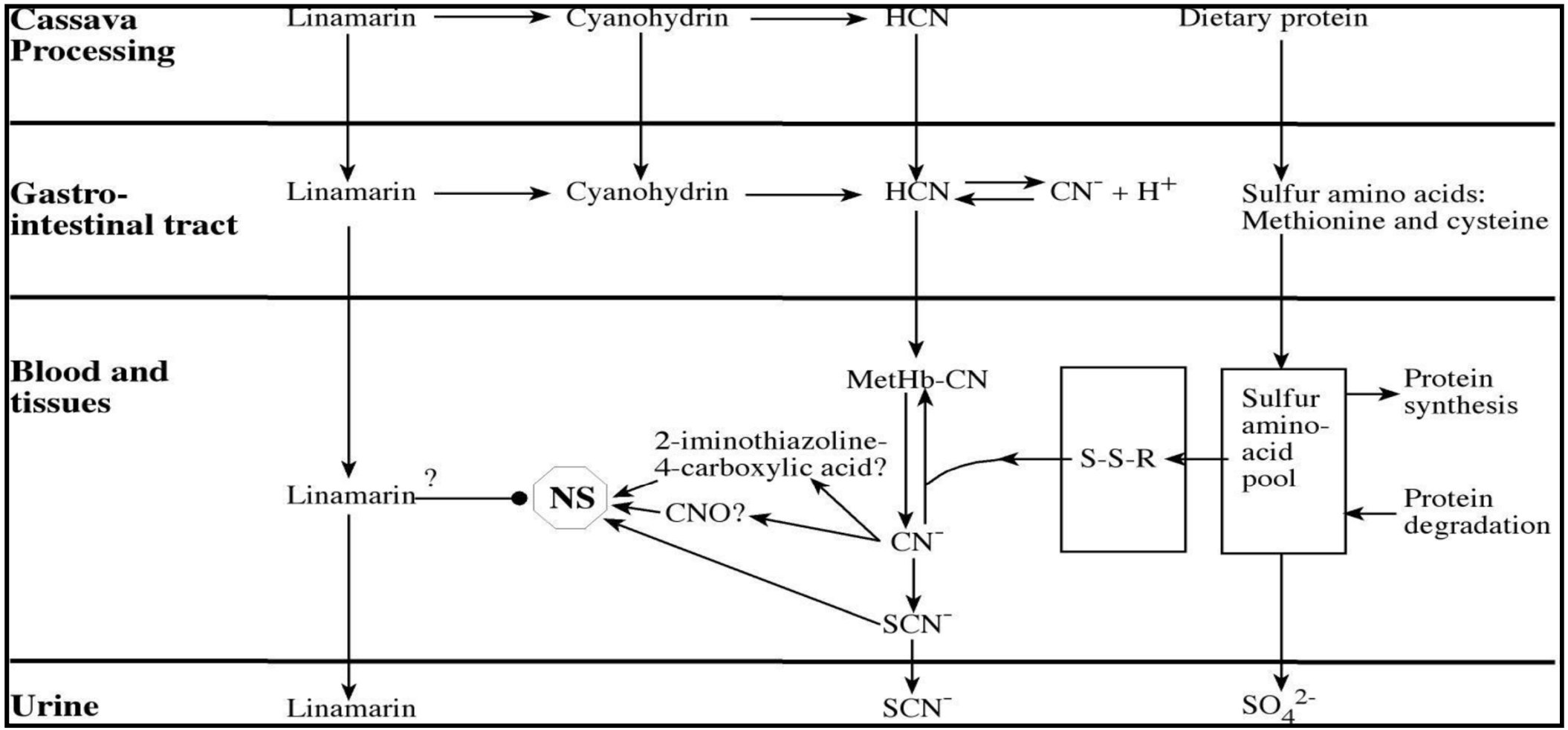
**Vulnérable Subjects: mainly women of childbearing age, people with low education who are unaware of the toxicity of bitter cassava, or children over two years of age in full emotional, social and cognitive development.**

Hipolito Nzwalo, Julie Cliff. Konzo: From Poverty, Cassava, and Cyanogen Intake to Toxico-Nutritional Neurological Disease. www.plosntds.org June 2011 ; 5(6) : e1051 405; Diasolua Ngudi D, Banea-Mayambu J-P., Lambein F., Kolsteren P. konzo and dietary pattern in cassava-consuming populations of Popokabaka, Democratic Republic of ongo. Food and chemical toxicology 2011; 49(3): 613-619

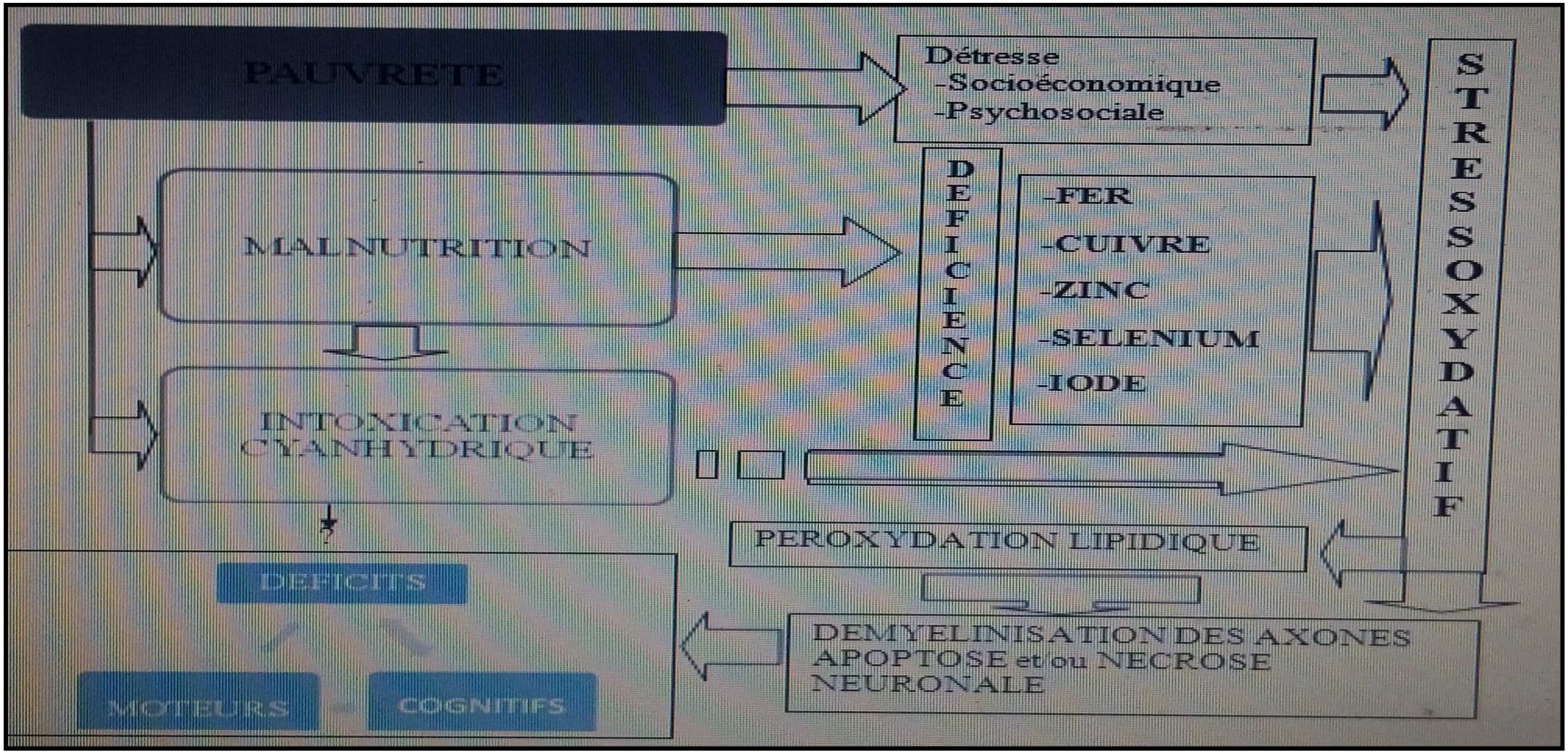
# Multiple and cumulative risks in neurodevelopmental health associated with konzo in sub-Saharan Africa.




Phenomenological model of multiple and cumulative risks in konzo?

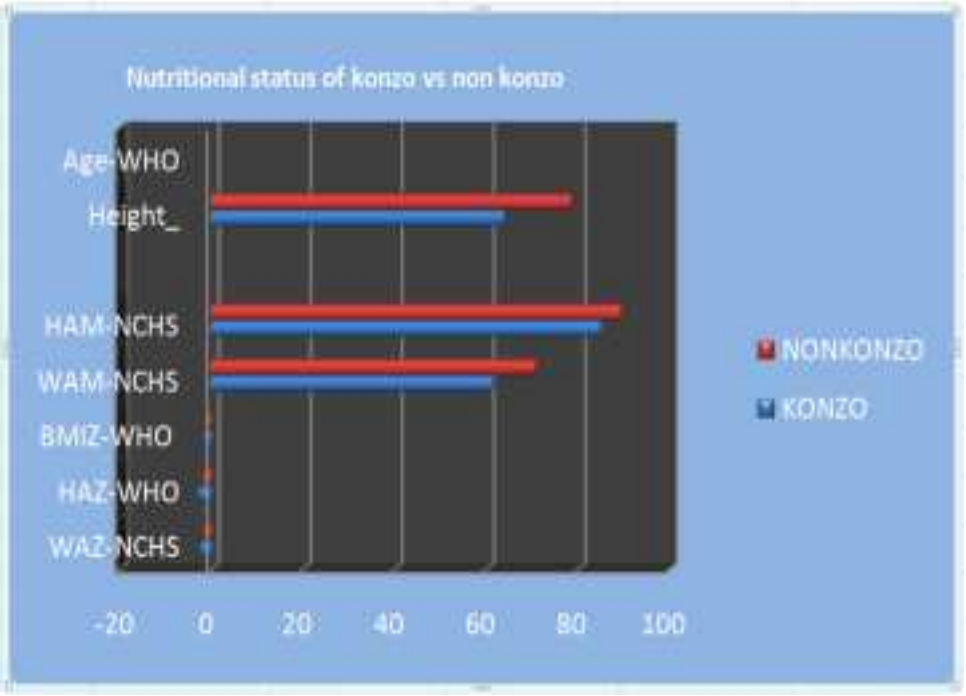


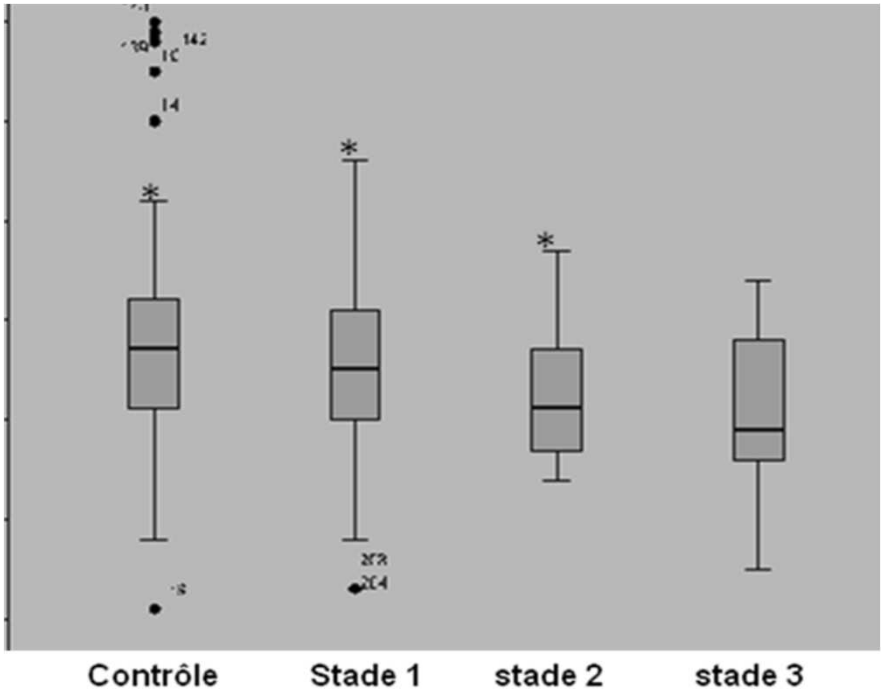

Tshala, OHSU, 2003




**Bumoko et al, 2016 : physiopathogénie des multiples et cumulatifs risques associés au konzo**

# Socio-economic and nutritional risks



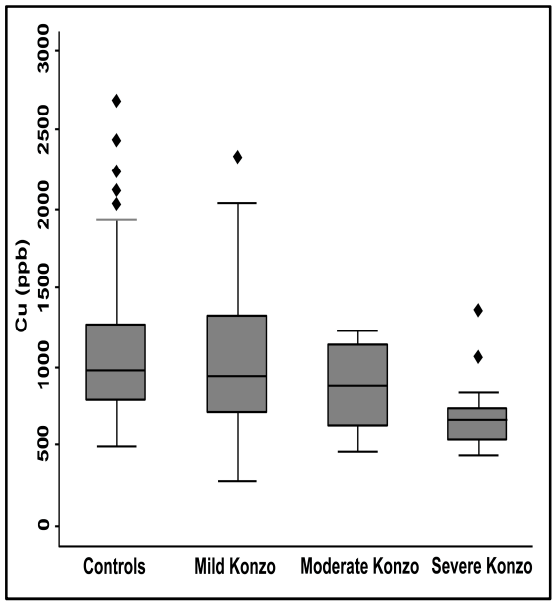




worse nutritional states based on Height for Age-WHO Z score (p<.001) and Weight for Age-WHO Z score (p=.020), Test of Students.

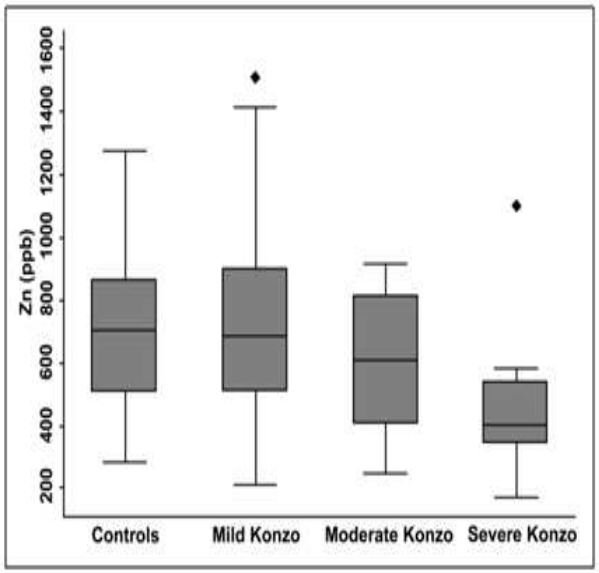
konzo severity was significantly associated with low quality of socio-economic family environment (HOME Scores) in Kuskal Wallis test, p=. 008).

Daniel Okitundu Luwa E-Andjafono, Guy Bumoko Makila-Mabe, Marie-Thérèse Sombo Safi Ayanne, Jackin Kambale. Kikandau, Nicole Mashukano, Théodore Kazadi Kayembe, Dieudonné Mumba Ngoyi, Michael Joseph Boivin, Jean-Jacques Tamfum-Muyembe, Jean-Pierre Banea Mayambu, Désiré Tshala-Katumbay.
Persistance des épidémies de konzo à Kahemba, République Démocratique du Congo: aspects phénoménologiques et socio-économiques. Pan African Medical Journal. 2014; 18:213
doi:10.11604/pamj.2014.18.213.4572

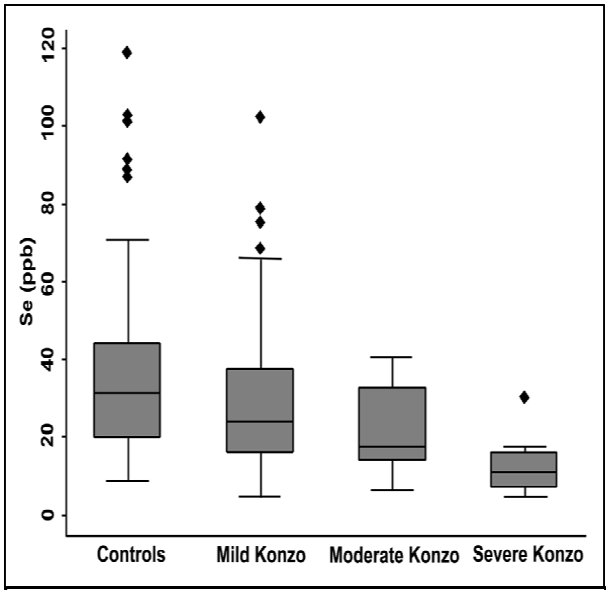
# Risks related to deficiency of oligoelements




Low level of serum Cu associated with severity of konzo




Low level of serum Zn associated with severity of konzo




Low level of serum Se associated with severity of konzo

**Lower serum levels of selenium, copper, and zinc are related to neuromotor impairments in children with konzo.**
**Bumoko, G M-M**; Sadiki, N H; Rwatambuga A; Kayembe K.P.; Okitundu, D L; Mumba Ngoyi, D; Muyembe J-J T; Banea, J-P; Boivin, M J; Tshala-Katumbay, D.
J Neurol Sci (2015), http://dx.doi.org/10.1016/j.jns.2015.01.007

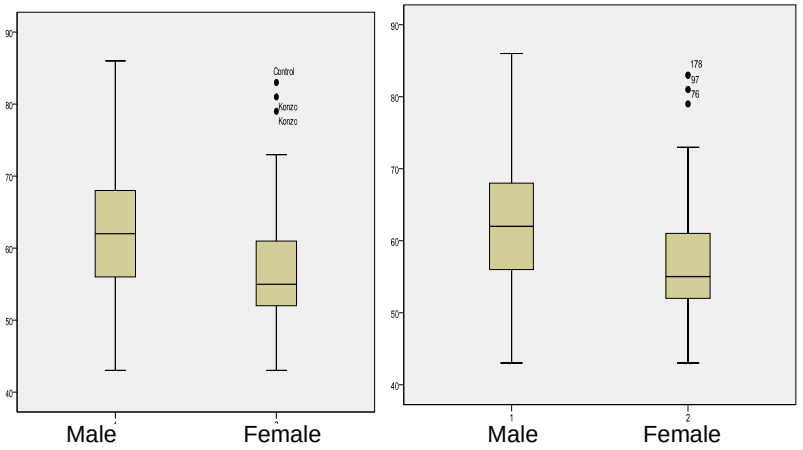
# Cognitive risks

| K-ABC II | Mild | Moderate | Severe |
|---|---|---|---|
| Mean (SD) | 59.4 (7.7) | 60.9 (9.5) | 52.6 (7.2) |
| Median (IQR) | 59 (52 - 65) | 62 (54 – 66) | 52 (45 – 56) |

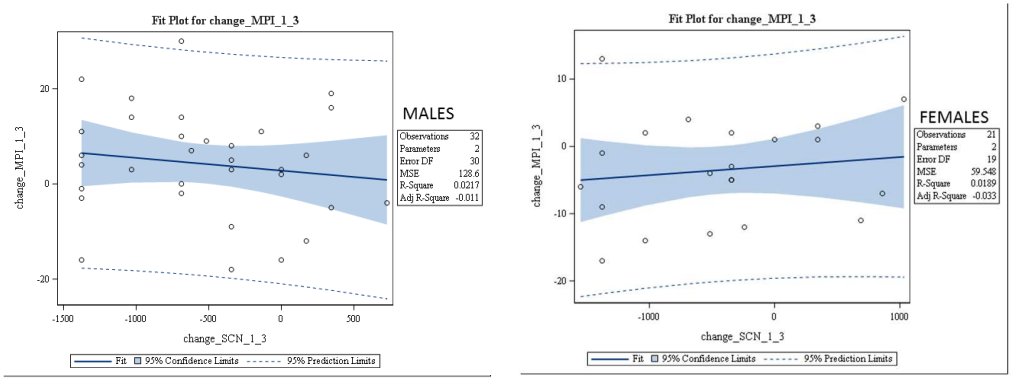
**KABC-II median scores changed with respect to disease status and severity.**
**However, significant differences were mostly noted between severely affected children and those with no or mild konzo (BOT-2 testing) and between severely affected children and the remaining groups (KABC-II testing) (*p < 0.01, Kruskall-Wallis test).***

Kambale KJ, Ali ER, Sadiki NH, Kayembe KP, Mvumbi LG, Yandju DL, Boivin MJ, Boss GR, Stadler DD, Lambert WE, Lasarev MR, Okitundu LA, Mumba Ngoyi D, Banea JP, Tshala-Katumbay DD. Lower sulfurtransferase detoxification rates of cyanide in konzo-A tropical spastic paralysis linked to cassava cyanogenic poisoning. Neurotoxicology. 2017 Mar;59:256-262. doi: 10.1016/j.neuro.2016.05.016. Epub 2016 May 28. PMID: 27246648

# Cognitive risks related to gender over the time




**MPI performances related to gender**




**Change in KABC-II MPI cognitive performance and change in urinary thiocyanate between baseline and 4-year follow-up.** Change in urinary thiocyanate and change in KABC-II MPI score for (A) boys with konzo and (B) girls with konzo. KABC-II=Kaufman Assessment Battery for Children, second edition. MPI=Mental Processing Index. DF=degrees of freedom. MSE=mean square error.

On base line, the male konzo children done better than female on total cognitive ability (MPI)

Consistent with baseline, both konzo and non-konzo boys declined on KABC-II MPI performance at 2- and 4-year follow-up (P< 0.01), but not the girls. No significant relationship between thiocyanate and KABC-II MPI cognitive ability performance

Michael J Boivin, Daniel Okitundu, Bumoko Makila-Mabe, Marie-Therese Sombo, Dieudonné Mumba, Alla Sikorskii, Banea Mayambu Desire Tshala-Katumbay Cognitive and motor performance in Congolese children with konzo during 4 years of follow-up: a longitudinal analysis. www.thelancet.com/lancetgh Vol 5 September 2017.; 17. MICHAEL J. BOIVIN, DANIEL OKITUNDU, GUY BUMOKO, THERESE SOMBO, DIEUDONNE MUMBA, THORKILD TYLLESKAR, CONNIE E. PAGE, J. J. TAMFUM-MUYEMBE, DESIRE TSHALA-KATUMBAY (2013). Neuropsychological Effects of Konzo: A Permanent Neuromotor Disorder from Insufficiently Processed Cassava. Pediatrics 2013; 131: e1231–e1239.

# Neurodegenerative risks: correlations between oxydative stress(8, 12-Isoprostane F2-VI ), nutritional biomarkers and with neuropsychogical abilities in konzo

1. Negative correlation with Serum Albumin (r de Spearman = -0,40 ; p=0,02) ;
2. Positive correlation with Serum Triglycérides (r de Speaman= 0,45 ; p<0,01)
3. Negative correlation with BOT-2 (Total neuromotor abilities) (r de Spearman = −0,41; p=0,02 )
4. Negative correlation with K-ABC II( MPI, Cognitive abilities) (r de Spearman = −0,61; p= 0,00)
5. Negative correlation with Se serum level (r de Spearman = - 0,75 , p < 0.01)

**Serum 8, 12-Isoprostane F2-VI marker of oxidative damage and cognition deficits in children with konzo.**
Makila-Mabe BG, Kikandau KJ, Sombo TM, Okitundu DL, Mwanza JC, Boivin MJ, Ngoyi MD, Muyembe JJ, Banea JP, Boss GR, Tshala-Katumbay D.
Metab Brain Dis 29: 359–366

# Conclusion

**Motor, cognitive, mood and behavior disorders existed together in konzo.**

**Are they comorbidities or Have they a common origin related to cyanide dietary intoxication?**

**Nevertheless, to present now ‘’konzo without intellectual disabilities” like in previous literature (WHO, 1996) becomes liable to be questioned ?**

**Further studies are needed for a new reading of natural history of konzo in biopsychosocial and neurodevelopmental perspectives.**

**In the best way to deal with konzo and to prevent it , we must revise WHO’s definition of konzo. We hope that GAPSYM have a role to play.**

**We are grateful to the Congo National Institute of Biomedical Research (INRB) and the National Nutrition Program (PRONANUT) for their technical and scientific assistance, the WHO for travel support, and the Fogarty International Center and the NIEHS, NIH, Bethesda, USA for Research support.**

**I thank  you for your attention**