

Onchocerciasis associated epilepsy in the DRC from 2014 to 2017

Michel Mandro

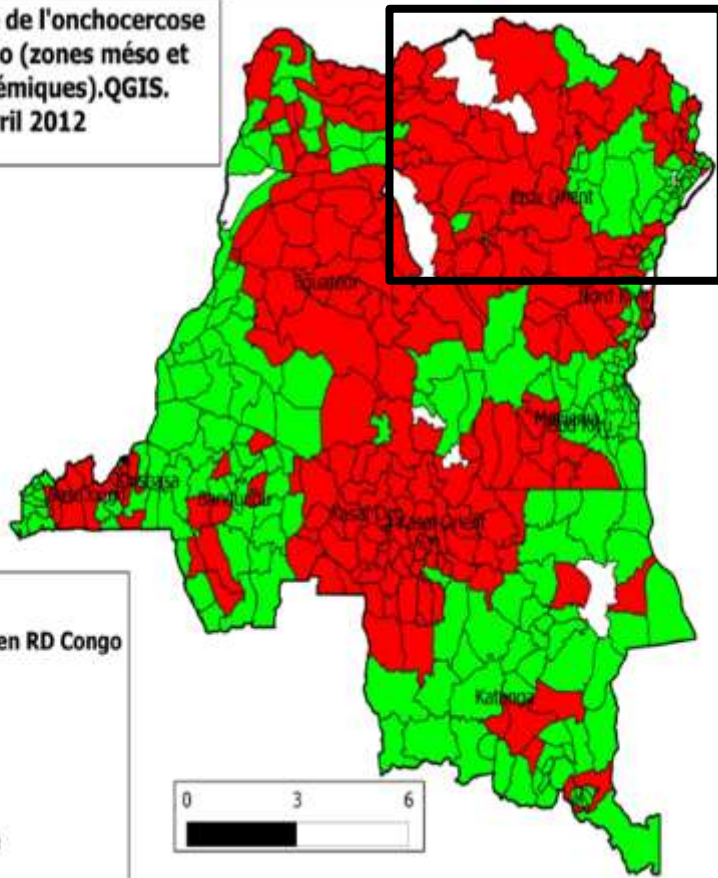
Division Provinciale de Santé de l'Ituri, DRC

Talk points

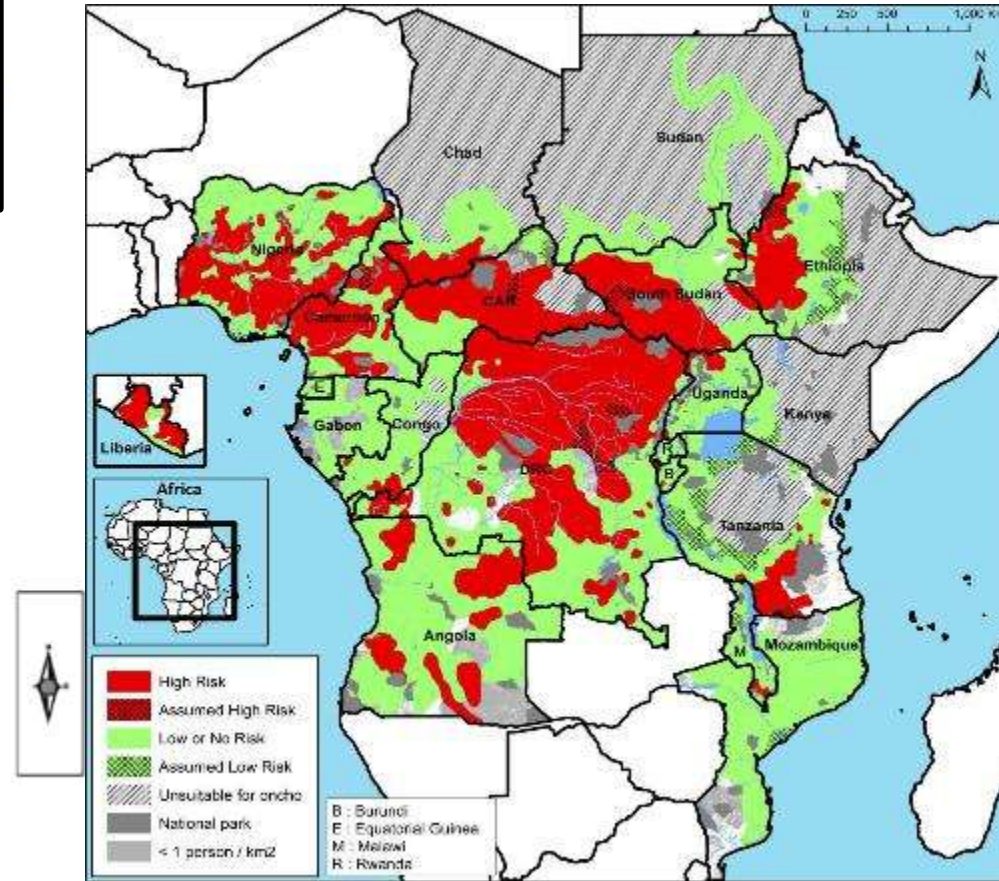
- 1. Onchocerciasis and DRC study sites**
- 2. Epilepsy prevalence studies**
- 3. Case - Control studies**
- 4. Clinical manifestations of OAE**
- 5. Interventions needed**
- 6. Conclusions**

The Orientale Province is an hyper endemic Onchocerciasis area in DRC

Cartographie de l'onchocercose en RD Congo (zones méso et hyperendémiques). QGIS. Avril 2012



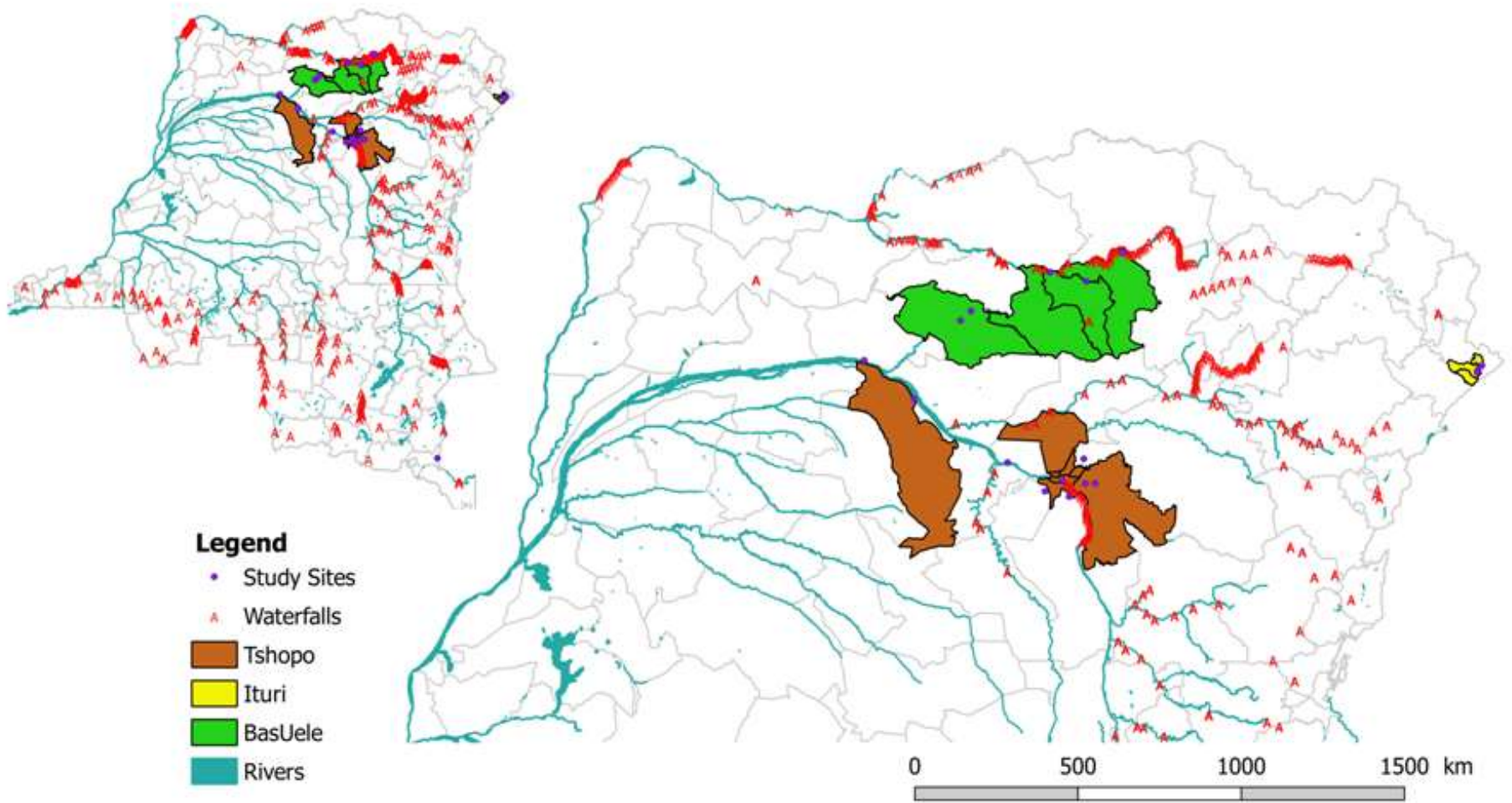
AFRICA DISTRIBUTION and RISK



DRC two thirds of the country are endemic for Onchocerciasis

14 millions infected in DRC (Tot Pop:70 million), 26 millions exposed

THREE STUDY SITES IN THE EX-ORIENTALE PROVINCE (2014-2017)



Methodology: prevalence studies 2014-16

- case of epilepsy defined as a patient who lost consciousness at least twice with seizures and without fever or any acute illness
- Community-based cross-sectional prevalence studies
- Door to door visit
- 3 different methodologies to select villages/households:
 1. 1 in 3 households interviewed per village
 2. All households interviewed
 3. 2-stage cluster sampling approach (Ituri)

Methodology: to identify persons with epilepsy

- Bas- Uele and Tshopo: house to house case detection by doctors
- Ituri: a three-stage approach was used:
 - In stage 1:** all household members screened for epilepsy by villages workers using 5 screening questions (J.M Preux)
 - In stage 2:** a diagnosis of epilepsy was validated by a doctor
 - In stage 3:** confirmation of the epilepsy diagnosis by a neurologist

2014-16 epilepsy prevalence in door to door surveys in onchocerciasis endemic regions in the EX-ORIENTALE PROVINCE

Province (Sites)	Health zone	Health Area	Epilepsy prevalence (%)
Ituri	Logo	Draju	6.2%
	Rethy	Rassia	3.6%
		Lokpa	3.7%
Bas Uélé	Aketi	Wela	6.8%
		Makoko	8.4%
Tshopo	Yahuma	Mombongo	2.1%
	Tshopo	Makutano Pumuzika	7.4%
	Yaleko	Yatange	2.6%
	Wanierukula	Salambongo	2.6%
		Makana	0.8%

Prevalence rates of epilepsy, onchocerciasis (O.v.) endemicity, years of Ivermectin distribution and Ivermectin coverage in the 3 study sites

Health Area	Population Surveyed	Epilepsy prevalence	Epilepsy of recent onset	O.v. nodules	O.v. skin lesions	Years of Ivermectin distribution	Ivermectin coverage 2014
Draju	1063	6.2%	1.0%	22.2% ²	0.5%	0	0%
Rassia	898	3.6%	0.3%	27.3% ²	0.2%	3	87.8%
Lokpa	846	3.7%	0.4%	13.8% ^{2*}	0.0%	3	73.0%
Yahuma	1259	2.1%	0.02%	57% ^{3*}	0.1%	10	33.0%
Makutano Pumuzikia	203	7.4%	1.0%	94% ^{4*}	2.0%	9	17.6%
Yatange	424	2.6%	0.2%	67% ^{4*}	4.0%	4	3.5%
Salambongo	5657	2.6%	0.2%	17.1% ²	1.9%	10	14.4%
Makana	1121	0.8%	0	55% ^{4*}	0.4%	10	13.6%
Wela	570	6.8%	1.1%	98% ⁵	9.7%	13	65.1%
Makoko	367	8.4%	1.4%	98% ^{5*}	3.3%	13	78.1%

Methodology: case - control studies

Titule : controls of same age group chosen by convenience among persons without epilepsy

Salambongo and Ituri: age matched controls chosen at random

All areas: Nested age, sex and village matched case-control study using prevalence study data

TITULE : case control study (June 2014)

Characteristics	Cases	Controls	OR (95% CI)	P-value
Mean body weight, Kg (SD)	38.9 (11.2) (n=58)	46.7 (15.2) (n=23)	0.96 (0.91 – 1.00)	0.06
Mean height, <i>cm</i> (SD)	148 (15) (n=58)	154 (18) (n=22)	0.98 (0.94 – 1.02)	0.4
Onchocerciasis skin lesions	12/41 (29%)	1/56 (4%)	10.32 (2.04 – 52.26)	0.005
Itching	26/40 (65%)	8/51 (16%)	11.22 (3.83 – 32.82)	<0.001
Skin nodules	3/40 (8%)	2/46 (4%)	1.13 (0.14 – 9.29)	0.9
Burn scars	10/57 (18%)	0/61 (0%)	^d	0.001

TITULE: case control study (June 2014)

Characteristics	Cases	Controls	P-value
Skin snip OV PCR pos	26/34 (76%)	10/14 (71%)	0.7
OV16 pos	39/49 (78%)	15/18 (83%)	0.5
<i>Mansonella perstans</i> PCR pos blood	39/49 (78%)	13/20 (65%)	0.91
<i>Loa Loa</i>	1	1	0.91
<i>Taenia solium</i> AB	neg	neg	
<i>Toxocara</i> AB	neg	neg	
<i>Trypanosoma</i> sp AB	neg	neg	
Ivermectin use last round	29/59 (49%)	29/61 (48%)	0.8

ITURI: case control study (October 2015)

	Persons with epilepsy		Controls	
Health Area	Drazu	Rassia	Drazu	Rassia
Number of years IVM	0	3	0	3
Biopsy pos (MF)	55.9%	50%	29%	12.5%
Mean MFL	33.6	21.5	3.8	2.7
OV16 pos	45.7%	45.8%	26.0%	18.7%

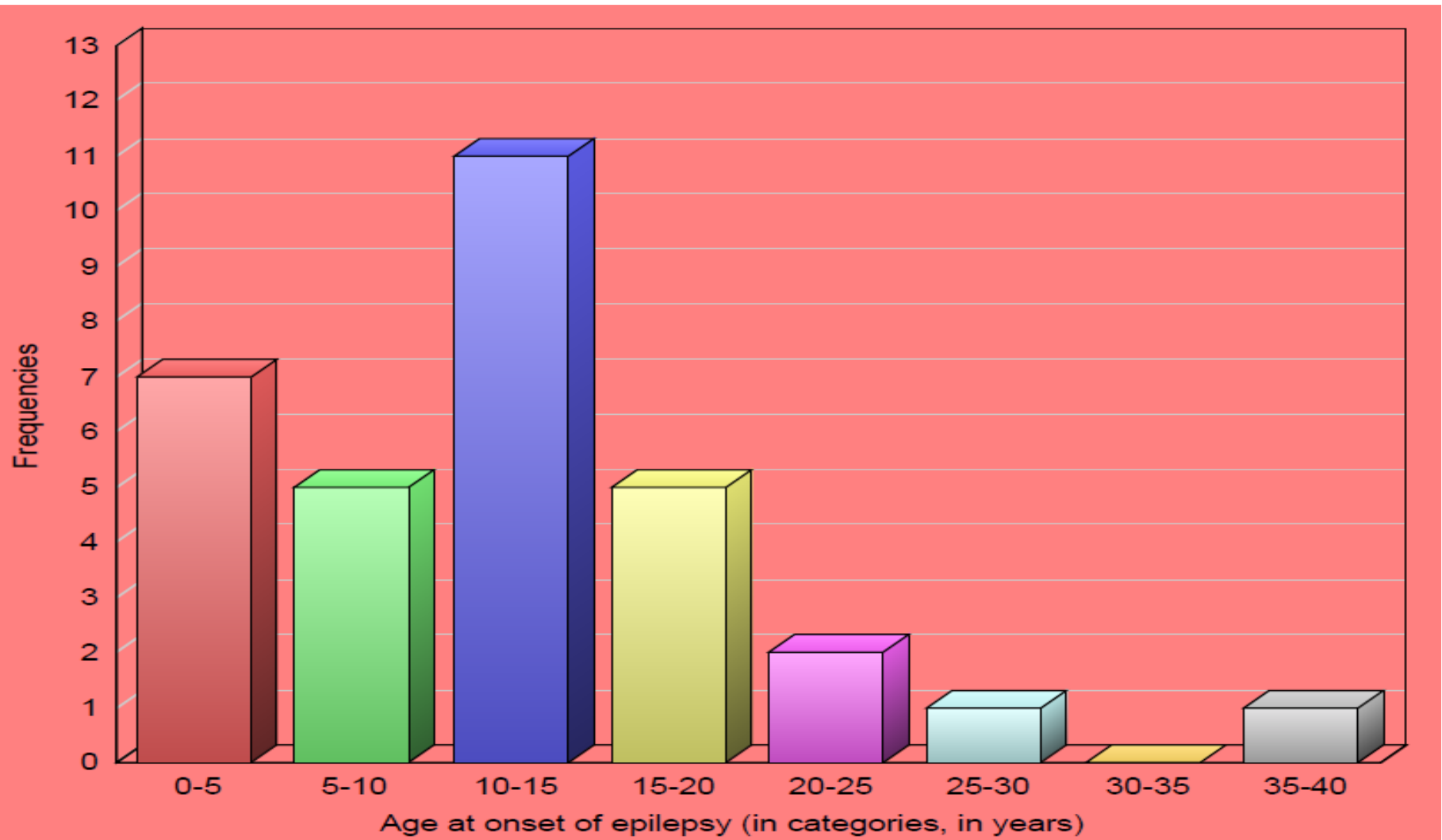
Village, age, and gender matched nested case and control study: 96 cases and 96 controls (chosen from 12.366 people)

Factor	Odds Ratio	95% C.I.	P Value
Ivermectin received the year before epilepsy appeared (equivalent year in the controls)	0.52	0.28, 0.98	0.04
Proportion of occasions, in years eligible, Ivermectin received after epilepsy appearance (or equivalent period in controls)	0.89	0.46, 1.70	0.71

Clinical aspects of OAE

- Onset of seizures between the age of 5 to 20
- Most people with epilepsy presented with general tonico-clonic seizures
- Epilepsy with atonic neck seizures(nodding) observed in Aketi and Ituri
- Nakalanga features observed in most study sites

Logo Health zone in Ituri: age at onset of epilepsy



Stunted growth (“Nakalanga syndrome”)

26 years old women, 26kg, 1m27,
Salambongo, Tshopo, DRC



20 years old, 31kg, 1m41, Logo, Ituri DRC,
with his brothers 17years and 8years old

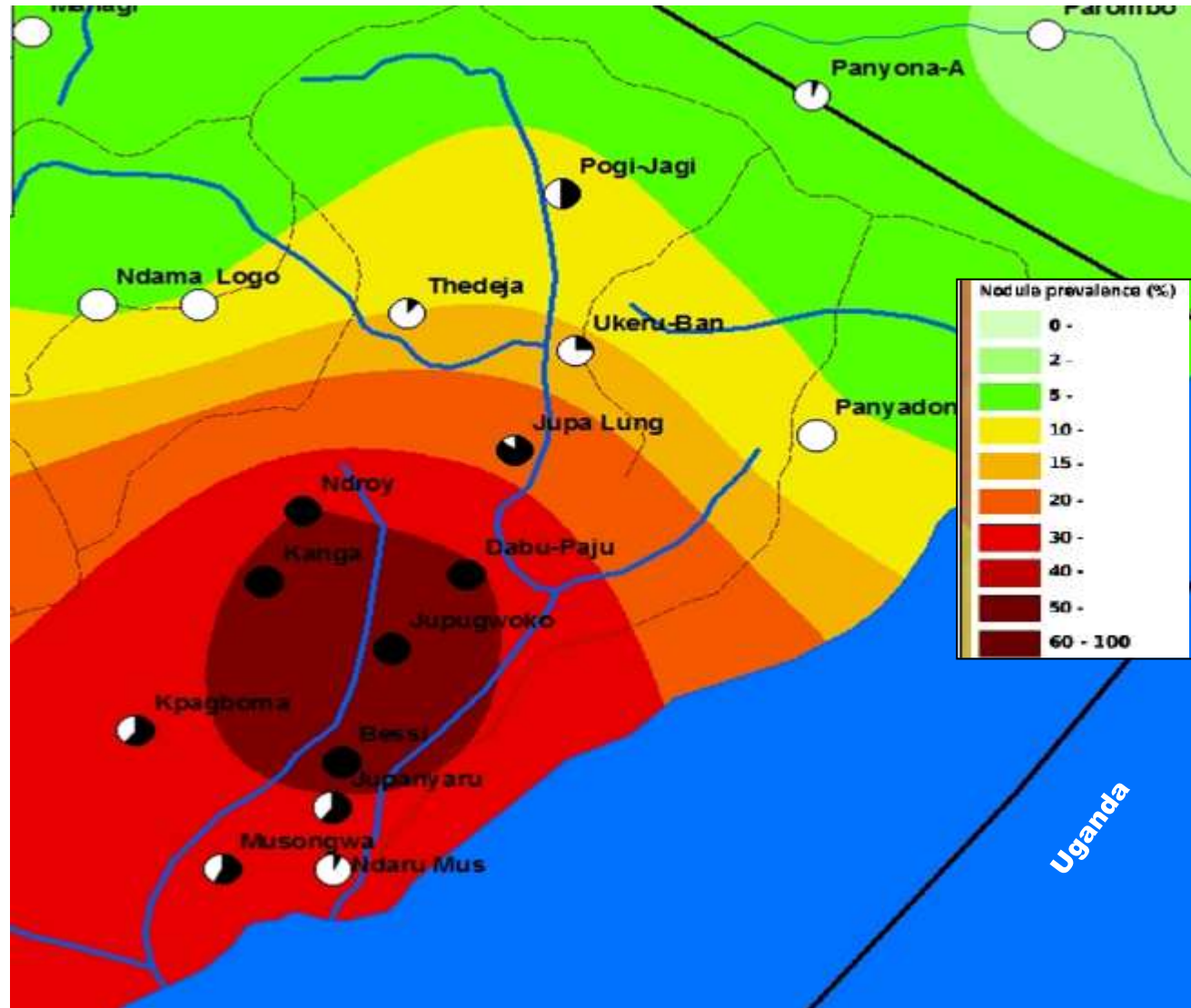


Mean mf load : 155/ml

OAE is a major public health problem in areas where onchocerciasis is not controlled → need for interventions to be tested

- Ivermectin mass drugs distribution to prevent the occurrence of new cases of OAE
- Ivermectin to reduce the frequency of seizures in persons with OAE

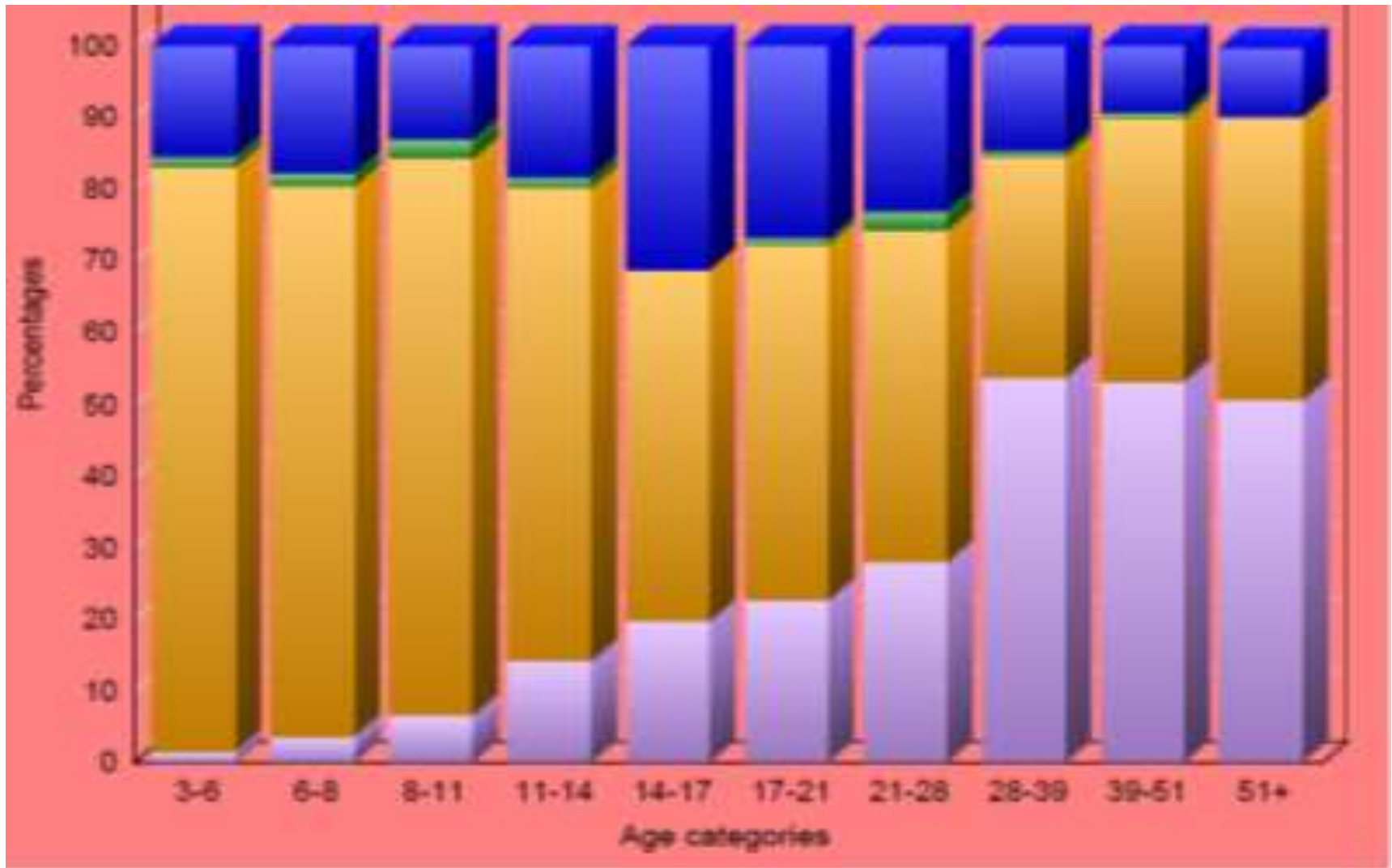
Study site for interventions: Logo health zone in Ituri



Epilepsy: 6.2%
NEVER
IVERMECTINE



OV16 positivity according to age group



Entomologic studies 2015-2017



Onchocerciasis situation in Logo health zone in Ituri

- Current low transmission of onchocerciasis possibly because of the deforestation
- Logo health zone not an ideal study site to investigate bi-annual IVM distribution to decrease the incidence of OAE
- Logo health zone ideal place to test the effect of IVM on seizures

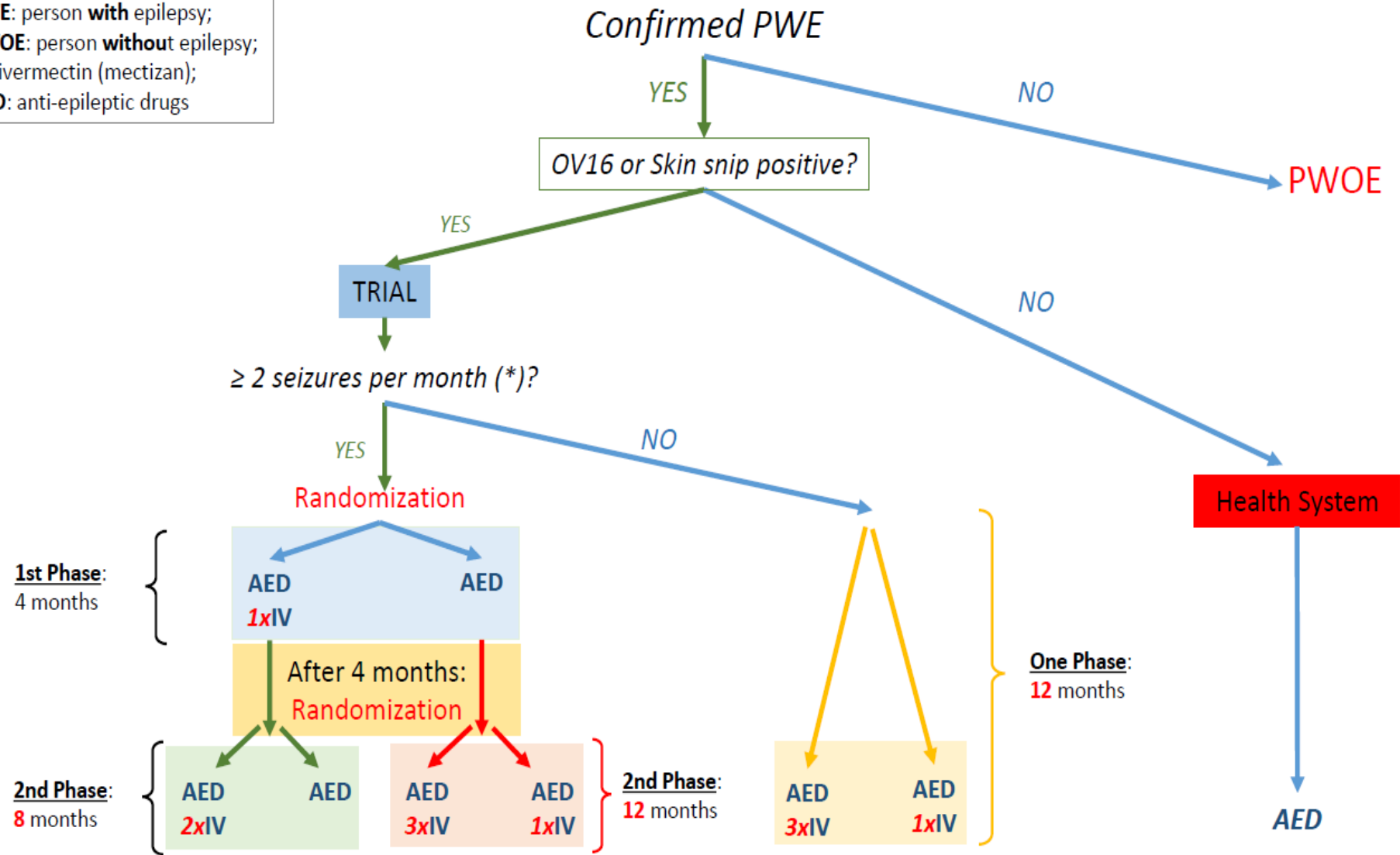
Ivermectin may decrease OAE seizures

- Between 2010-2011, a study comparing Moxidectin versus Ivermectin in subjects infected with OV was conducted in the same site of Logo Health zone
- After Moxidectin/Ivermectin single dose administration, 6 of 7 patients with onchocerciasis associated epilepsy became seizure free during 18 months
- Seizures reappeared when microfilaria reappeared

Age, gender	Age onset epilepsy	Seizures/months before IMP	Total nb seizures during 18 m	Seizures in 2015	Mf/mg skin snip during trial, 2010-12				Mf/mg skin and Ov16 in 2015		
					30 days before IMP	M1	M6	M12	M18	Mf	OvlgG4
26 M	9	2	3	7/month	21	2.3	1.6	9.8	13.8	13.5	+
25 M	15	2	0	4/year	55	3.0	13.1	16.3	22.4	81	+
22 M	11	2 à 4	0	1 in 2 years	63	0	0	0	1.9	ND	ND
24 M	14	2	0	2/month	42	0	0	0.4	0.4	0	+
21 M	16	1	0	1/month	53	0	0	0	13.2	33	+
23 M	NK	NK	0	Died	19	0	0	0	2	Died	
21 M	NK	NK	0	Died	28	0	0	0	4	Died	

Pilote study to treat all persons with epilepsy in Logo health Zone, Ituri

PWE: person **with** epilepsy;
PWOE: person **without** epilepsy;
IV: ivermectin (mectizan);
AED: anti-epileptic drugs



Conclusions

- High prevalence of epilepsy in onchocerciasis endemic regions in the DRC
- Ivermectin may prevent OAE
- Can Ivermectin decrease the frequency of seizures in person with OAE?
- Strengthen Onchocerciasis elimination efforts
- More advocacy is needed to improve treatment/care of patients with epilepsy in Africa

NSETHIO



European Research Council
Established by the European Commission



