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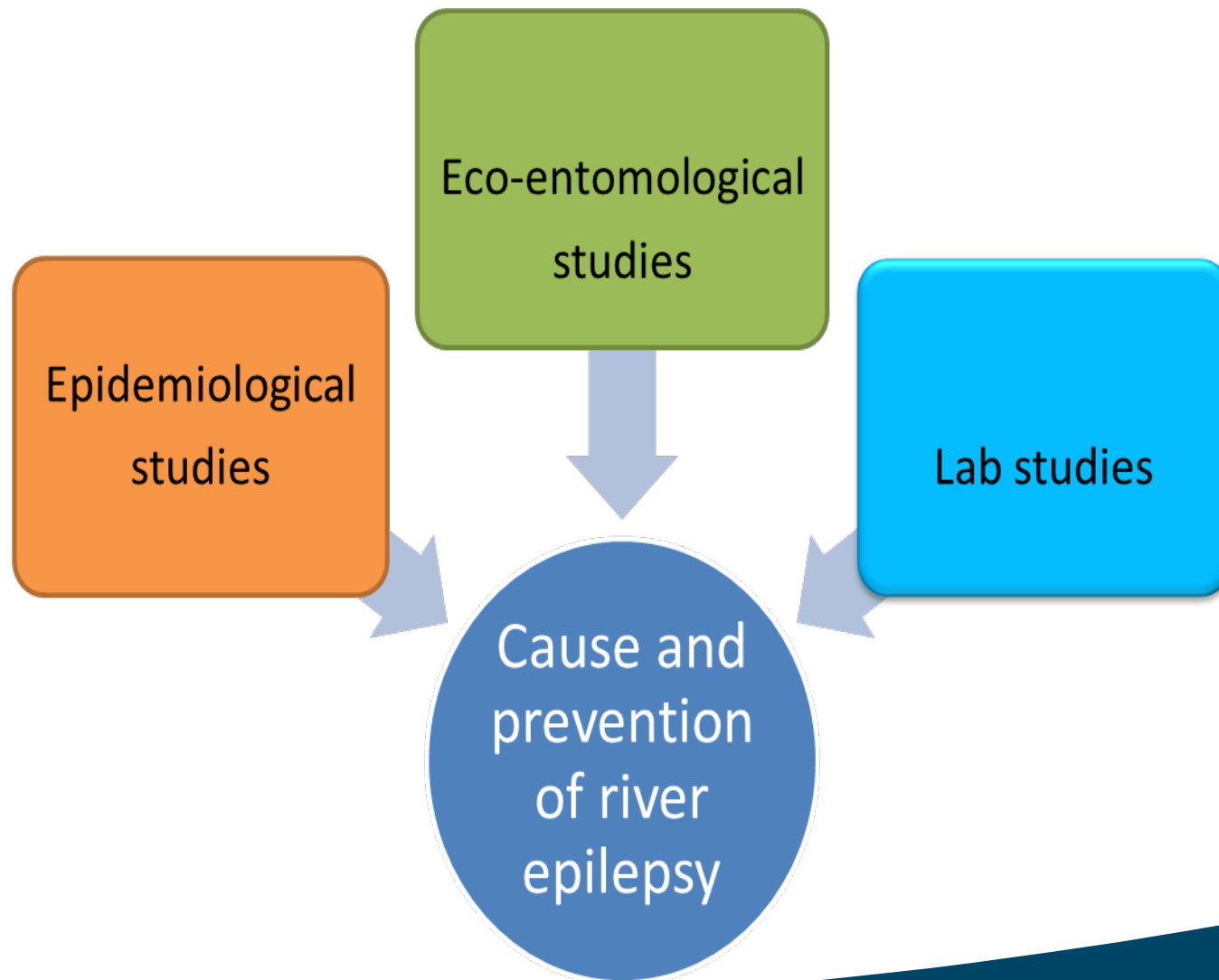
# NSETHIO project

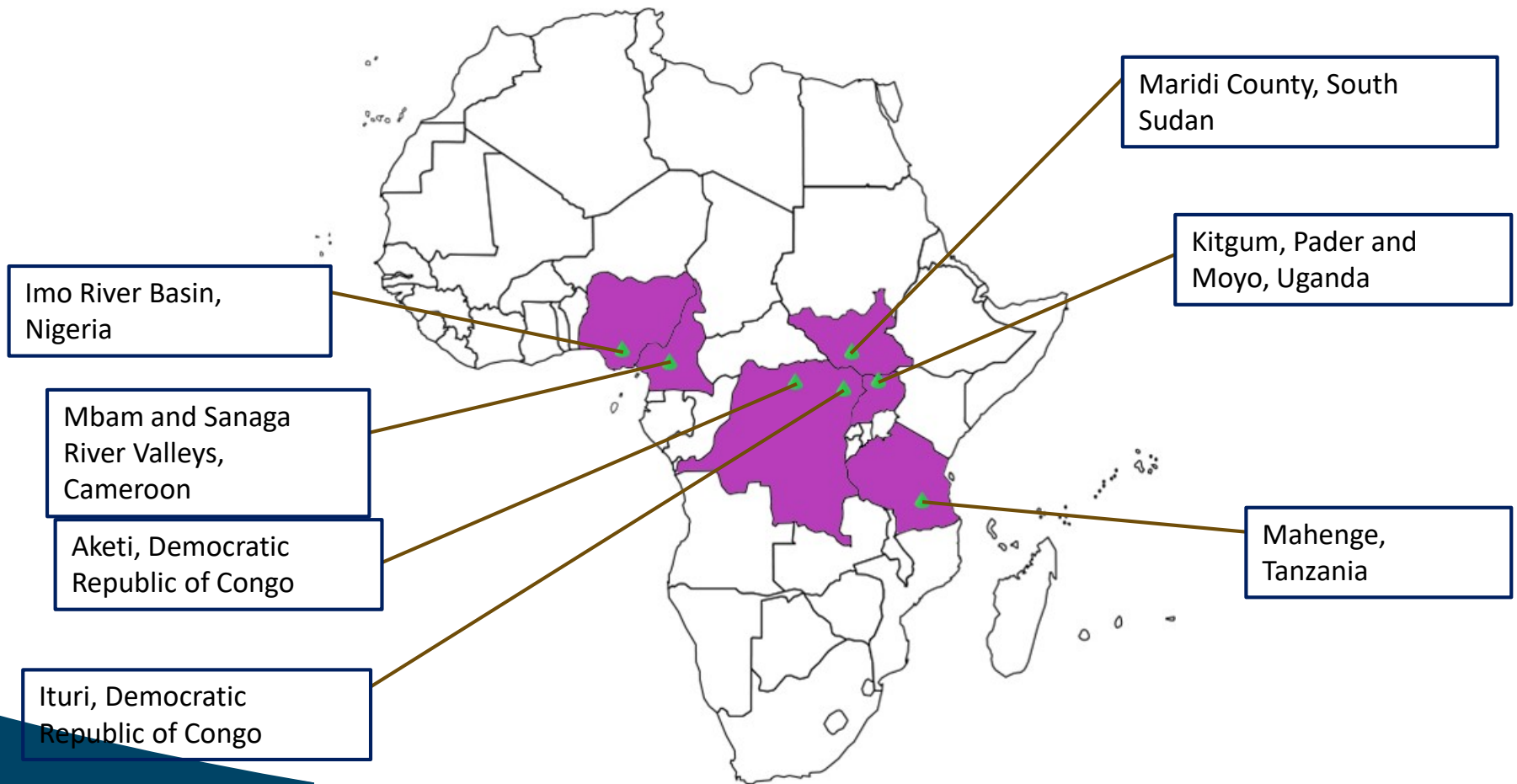
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# Multi-country study in onchocerciasis endemic regions





# High prevalence of epilepsy in onchocerciasis endemic regions

Province	Health zone	Health Area	Epilepsy prevalence	Most likely explanation
Ituri	Logo	Draju	6.2%	Never ivermectin distribution
	Rethy	Rassia	3.6%	
		Lokpa	3.7%	
Bas Uélé	Aketi	Wela	6.8%	Very high exposure to blackflies
		Makoko	8.4%	
Tshopo	Yahuma	Mombongo	2.1%	
	Tshopo	Makutano	7.4%	Very low treatment ivermectin coverage
	Yaleko	Yatange	2.6%	
	Wanierukula	Salambongo	2.6%	

Median epilepsy prevalence in africa : 1.4‰ (Preux & Druet-Cabanac, Lancet Neurol 2005)



# High incidence of epilepsy associated with high ongoing transmission of *O. volvulus* despite 14 years CDTI

	Wela		Makoko	
Age (years)	Nb examined	OV16 pos (Nb,%)	Nb examined	OV16 pos (Nb,%)
7	60	46 (77%)	43	19 (44%)
8	43	33 (77%)	35	18 (51%)
9	21	18 (86%)	17	6 (35%)
10	28	25 (89%)	35	17 (49%)
All ages	152	122 (80%)	130	60 (46%)

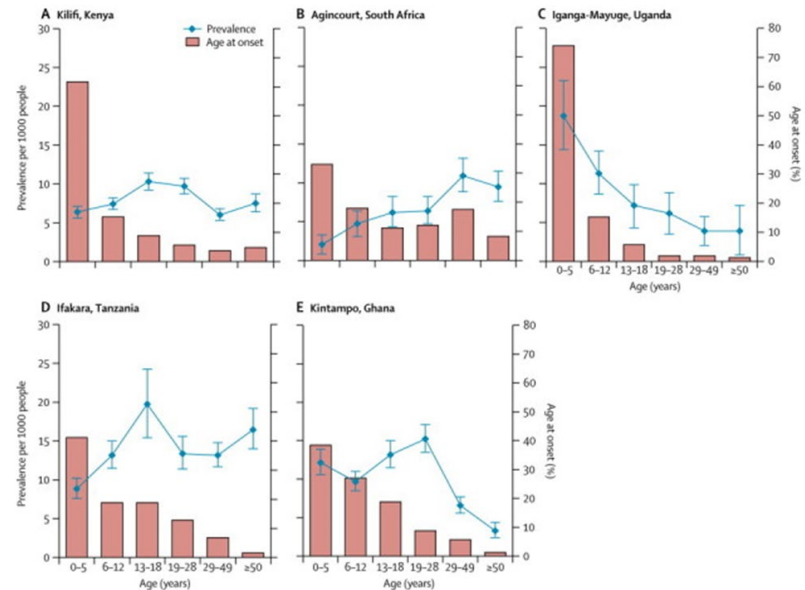
# DRC: Age and sex matched case control studies comparing area with and without CDTI

	Cases		Controls		
	Draju, Logo (Ituri)	Salambongo, Wanierukula (Tshopo)	Draju, Logo (Ituri)	Salambongo, Wanierukula (Tshopo)	P value*
<b>Skin biopsy test positive</b>	56% (33/59)	79% (53/67)	26% (17/65)	67% (36/54)	0.001 0.2
<b>Mean (range) mf load</b>	31.79 (0-352.00)	27.88 (0-204.50)	2.74 (0-78.00)	18.50 (0-132.00)	<0.001 0.2
<b>O volvulus IgG4 antibodies</b>	51% (30/59)	42% (28/67)	22% (14/65)	44% (26/59)	<0.001 0.9

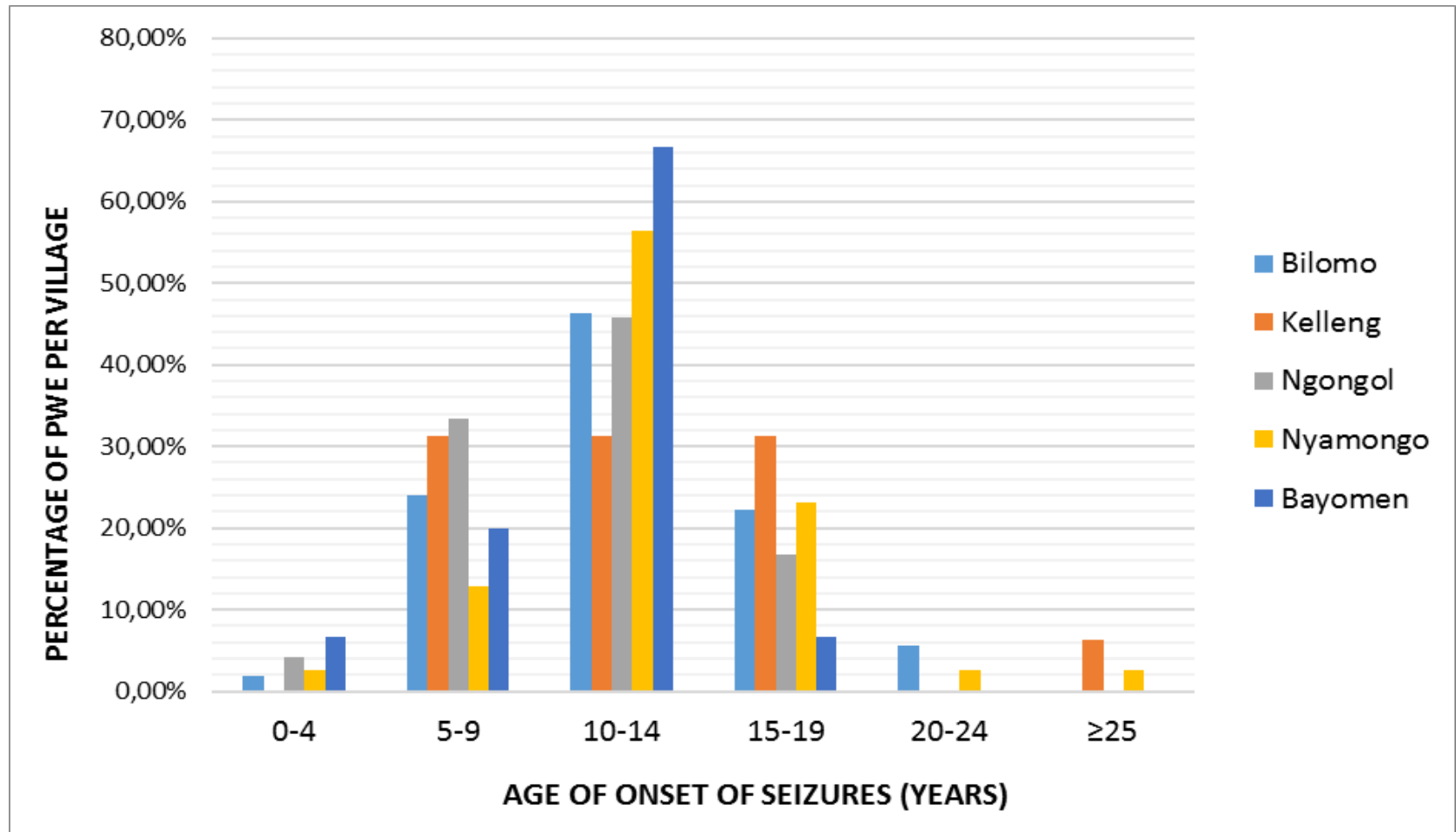
# Onset of seizures in persons with epilepsy in Africa

Onchocerciasis endemic regions

Non-onchocerciasis endemic regions



# Onset of epilepsy in Mbam and Sanaga valley, Cameroon: suggests high OAE prevalence

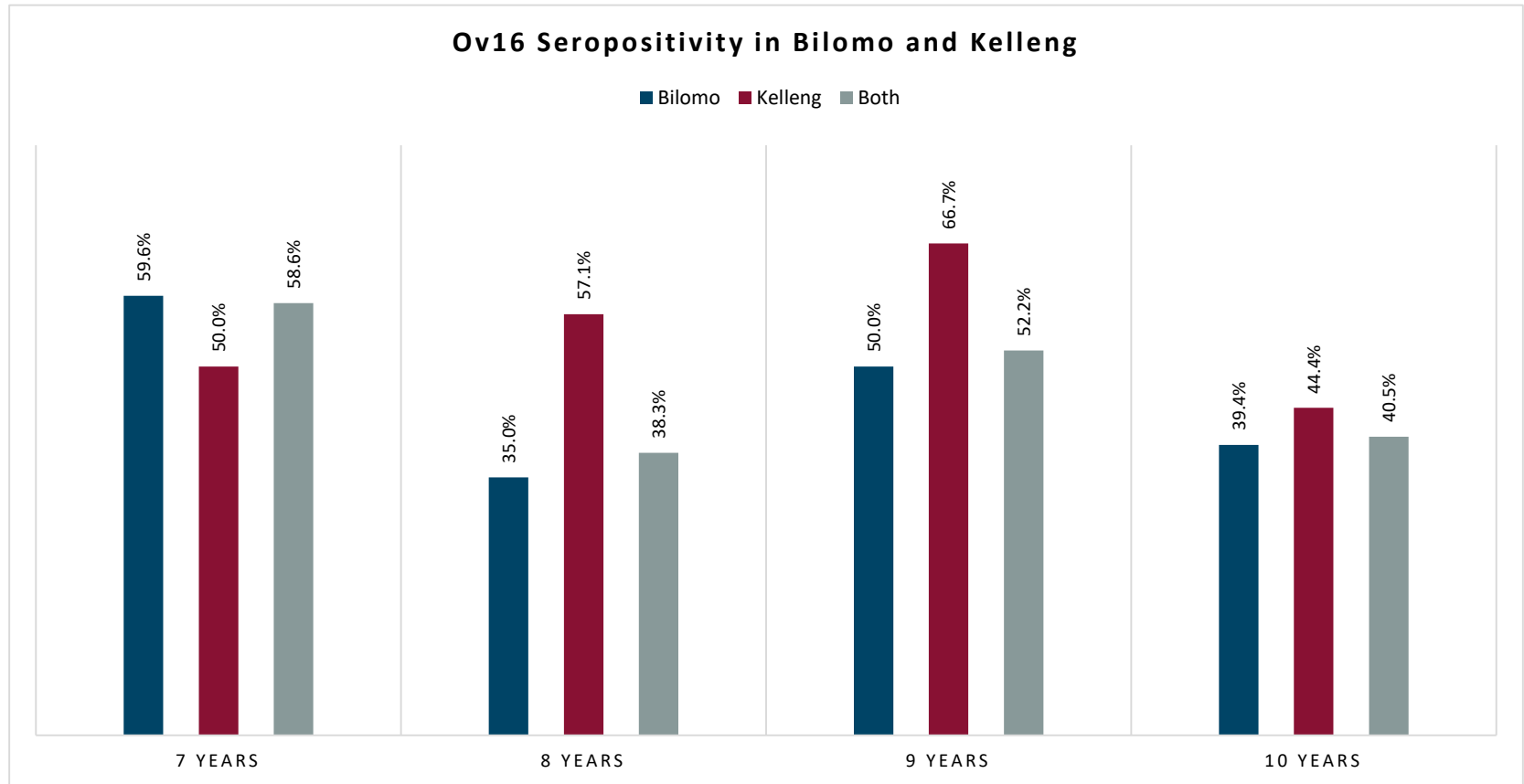




# Cameroon: age shift of persons with epilepsy to older age groups after 19 years CDTI because of decreased incidence of OAE

Characteristic	Bilomo 1998	Bilomo 2017
Overall prevalence	4.9%	4.6%
Nodding syndrome	NA	9
Age groups	(n = 93)	(n = 61)
• 5 – 9	3.23%	1.6%
• 10 – 14	20.43%	9.8%
• 15 – 19	39.78%	18.0%
• 20 – 24	25.81%	24.6%
• 25 – 29	4.30%	14.8%
• 30 – 34	4.30%	21.3%
• 35 – 39	2.15%	8.2%
• ≥ 40	0%	1.6%

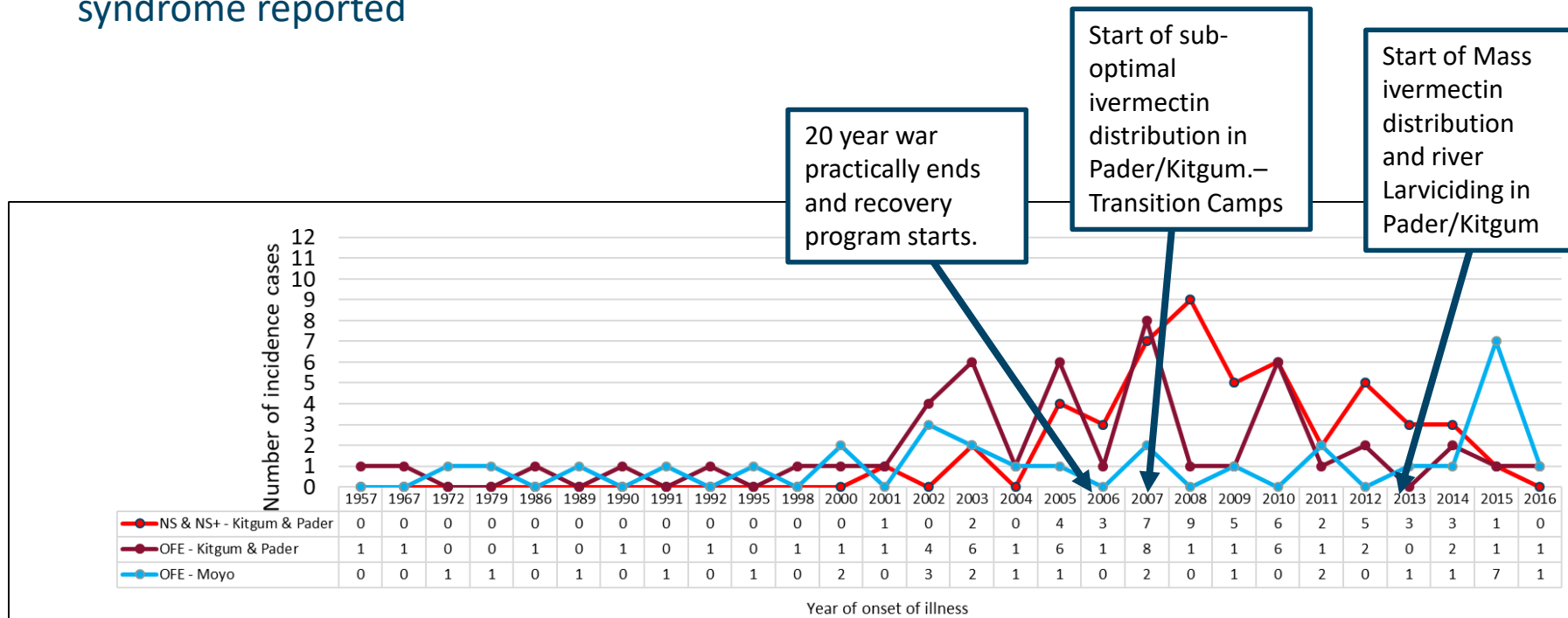
# Cameroon, Mbam and Sanaga valey despite 19 years CDTI still high ongoing *O. volvulus* transmission



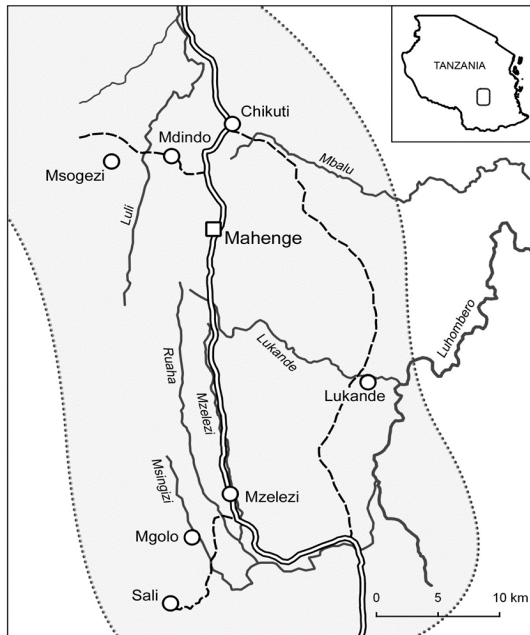
# Onchocerciasis elimination programs can successfully reduce epilepsy

## Northern Uganda: mass distribution of Ivermectin

- Nodding syndrome decreased with annual distribution
- Bi-annual distribution + larviciding: No new cases of nodding syndrome reported



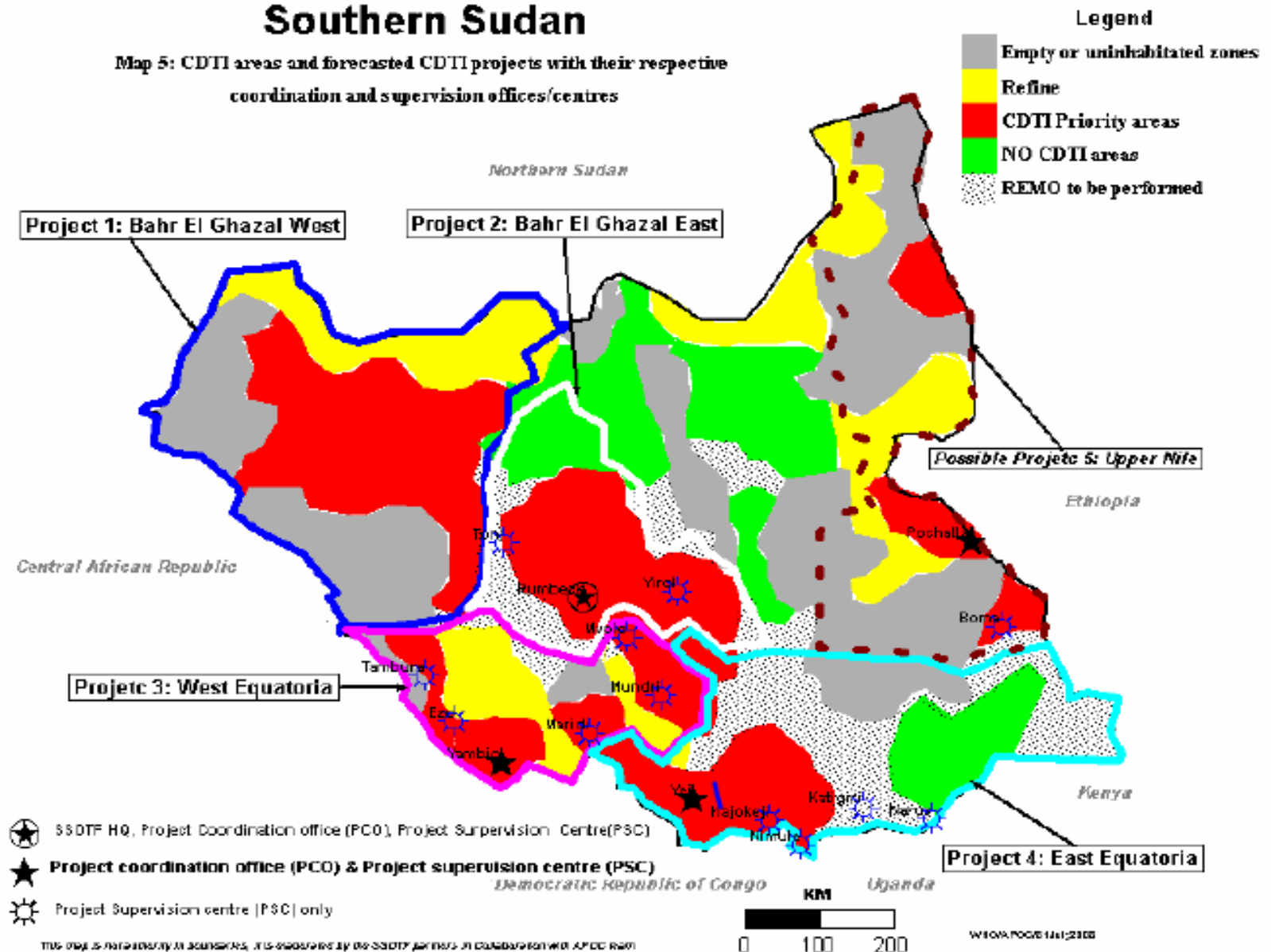
# Mahenge, Tanzania: high OAE prevalence in rural villages with high ongoing *O. volvulus* transmission



Village name	Population studied	Prevalence of epilepsy, n (%)	Prevalence of oncho (6-10yrs) [%]	Infective L3 stage (%)*
Mdindo	941	33 (3.51)	34.1	0.72
Msogezi	1558	55 (3.53)	40.7	0.37
Mzelezi	1775	51 (2.87)	5.3	0.62
Sali	1203	43 (3.57)	18.8	1.65
Matumbala	972	16 (1.65)	3.5	
Vigoi	1646	23 (1.40)	3.5	

# Southern Sudan

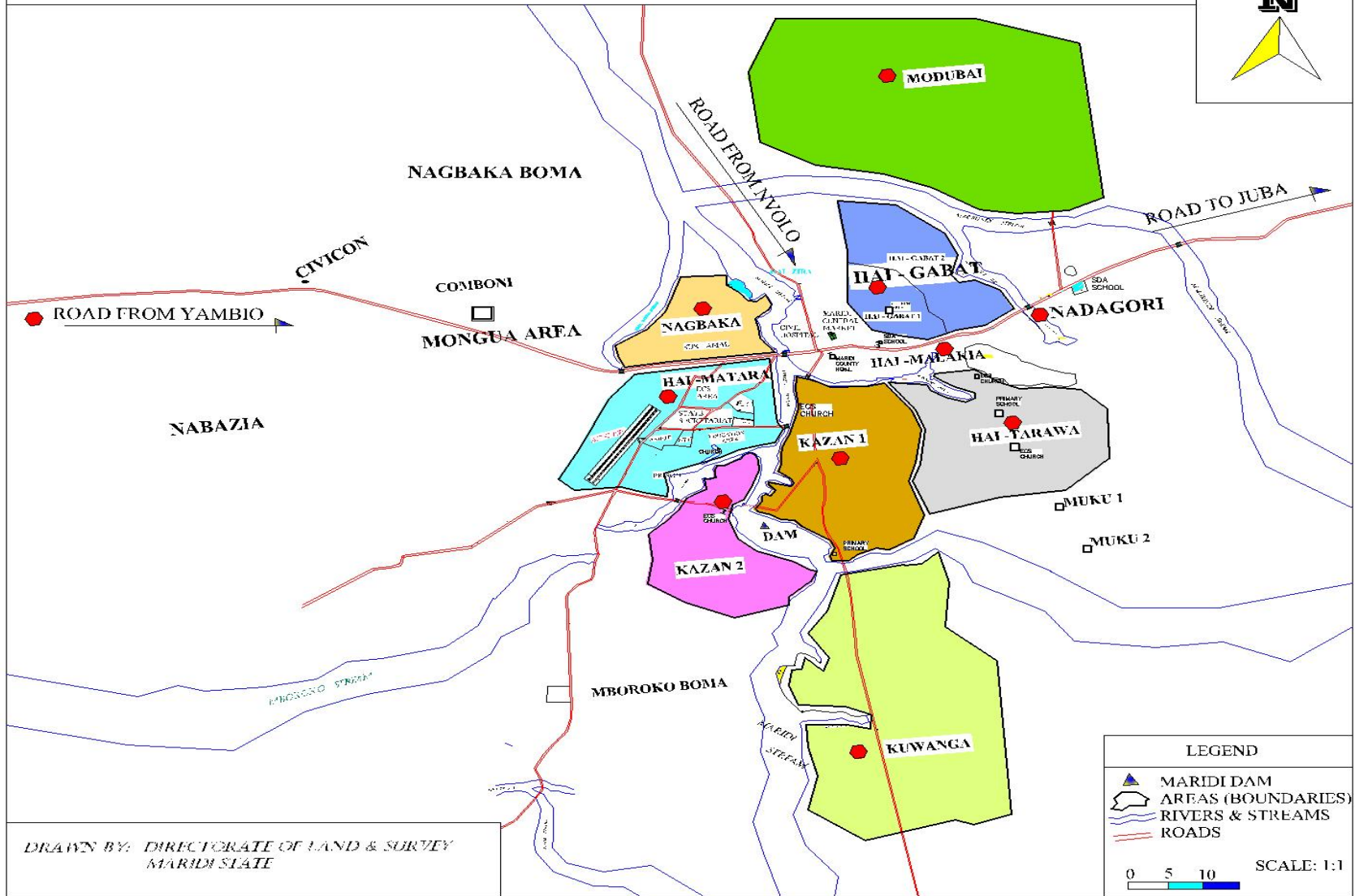
Map 5: CDTI areas and forecasted CDTI projects with their respective coordination and supervision offices/centres



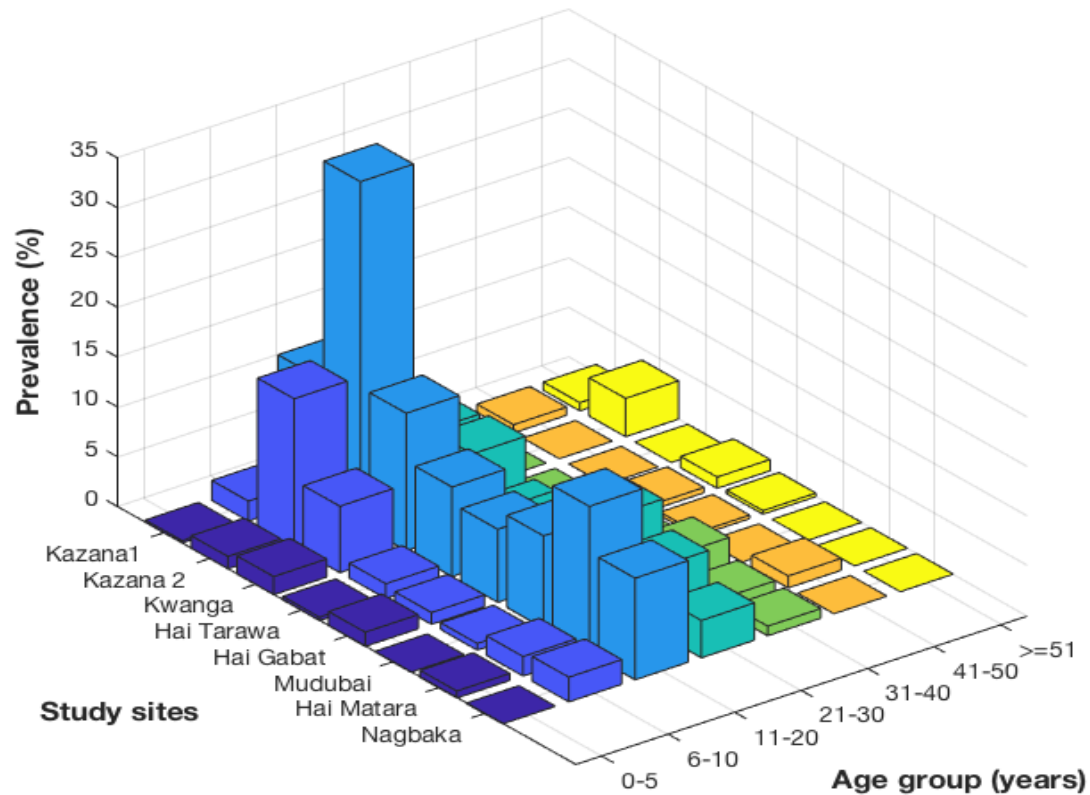
# May 2018 house to house epilepsy survey in Maridi, South Sudan

Study Area	Number of subjects interviewed	Number of confirmed epilepsy cases	Epilepsy prevalence	OR (90% CI)	P value
Kazana-1	2298	107	4.7		
Kazana-2	402	48	11.9	6 (1.8-3.7)	<0.001
Kwanga	273	16	5.9	1.4 (0.9-2.4)	0.2
Hai-Taiwara	5619	205	3.6	0.8 (0.6-1.0)	0.02
Hai-Gabat	4385	155	3.5	0.7 (0.6-0.9)	0.01
Mudubai	970	44	4.5	0.9(0.6-1.3)	0.6
Hai-Matara	2605	155	5.9	1.3 (1.0-1.6)	0.6
Ngabaka	1100	42	3.8	0.8 (0.6-1.1)	0.2

# MARIDI CENTRAL



## May 2018, epilepsy survey in Maridi, South Sudan: epilepsy prevalence per age group and study site





# OAE severe disabilities, Maridi, South Sudan

	History of Nodding seizures	Other forms of epilepsy	P-value*
<b>Cognitive disability</b>	275/229 (93.9%)	326/340 (96%)	0.09
<b>Thoracic, or spinal abnormality</b>	42/293(14.3%)	9/340 (2.7%)	<0.001
<b>Muscle wasting</b>	85/293(29.0%)	33/340 (9.7%)	<0.001
<b>Blindness One or both eyes</b>	11/293(4.8%)	0	
<b>Mean Rankin severe disability score (score &gt; 3)</b>	16/335 (4.8%)	10/401 (2.5%)	0.047

# Nakalanga features

Logo, Ituri, Democratic  
Republic of Congo



Mvolo, South Sudan



Cameroon



Uganda

**Normal H&E temporal cortex**



**Negative anti-tau temporal cortex (AT8)**

**Microglia frontal cortex (CD68)**

**Astrocytosis temporal cortex (GFAP)**

**Astrocytosis white matter (GFAP)**

**General histological findings:**

- Loss of Purkinje cells
- Cerebellum atrophy
- Hyperplasia Bergmann glia
- Neuronal loss
- Lymphocytes in the meninges

Case	Case 1		Case 2		Case 3		Case 4		Case 5	
Head noddins/other seizures	Head nodding followed by generalized convulsions; hallucinations and dizziness prior to convulsions		Head nodding triggered by the sight of food followed by convulsions		Generalized convulsions triggered by the sight of food		Head nodding		Head nodding	
qPCR data		qPCR		qPCR		qPCR		qPCR		qPCR
	Cerebellum cortex	+	Cerebellum cortex	+	Choroid plexus	+	Nervus opticus	-	Nervus opticus	-
	Nucleus dentatus	+	Cerebellum vermis	+	Olfactory nerve	+	Hippocampus	-	olfactory nerve	-
	Frontal cortex	-	Nervus opticus 2	+	Pons	-	Frontal base	-	Pons	-
	Hippocampus	-	Olphactory bulb	+	Nervus opticus	-	Pons	-	Medulla elongata	-
	Choroid plexus	-	Nucleus dentatus	-	Cerebellum vermis	-	choroid plexus	-	Vermis	-
	Olfactory bulb	-	Pons	-	Frontal cortex	-	Vermis	-	choroid plexus	-
	Pons	-	Frontal cortex	-	Thalamus + corpus mamillaria	-	Nucleus dentatus and cortex	-	Frontal cortex	-
			Hippocampus 1	-	Hippocampus	-	Frontal cortex	-	hippocampus	-
			Hippocampus 2	-					hypothalamus left	-
			Choroid plexus	-						
			Nervus opticus	-						
			Right corpus mamillaria	-						

# West Africa

**Tableau 2.** *Prévalence de l'épilepsie en Afrique subsaharienne par des enquêtes porte-à-porte*

Pays	Auteurs	Année	N <sup>1</sup>	P <sup>1</sup> ‰	IC 95 % <sup>2</sup>	U ou R <sup>3</sup>	Méthode	Déf	Commentaire
Côte d'Ivoire	Kouadjo	1990	309	74,0	43,0 - 105,0	R	ET	oui	65 % d'antécédents familiaux
Côte d'Ivoire (M'Brou)	Kaudjhis	1995	920	59,0	43,0 - 75,0	R	ET	oui	49 % d'antécédents familiaux
Cameroun (Bilomo)	Dongmo <i>et al.</i>	1998	1 900	58,0	46,9 - 69,1	R	ET	oui	
Nigéria (Aiyété)	Osuntokun <i>et al.</i>	1982	903	37,0	24,2 - 49,8	R	ET	oui	
Libéria	Goudsmit <i>et al.</i>	1983	4 436	28,0	23,0 - 33,0	R	ET	oui	
Bénin (Agbogbomé)	Gbenou	1995	530	24,5	10,9 - 38,1	R	ET	oui	

# Conclusion

OAE is major public health problem

OAE is a reason to strengthen onchocerciasis elimination programmes

OAE awareness will increase CDTI coverage

Onchocerciasis elimination programmes need to target regions with high OAE prevalence

Once a year CDTI has insufficient impact on incidence of OAE

Onchocerciasis elimination programmes need a morbidity management plan

# Post-mortem study Uganda

Case	Case 1		Case 2		Case 3		Case 4		Case 5	
Head noddins/other seizures	Head nodding followed by generalized convulsions; hallucinations and dizziness prior to convulsions (patient aware when about to convulse)		head nodding triggered by the sight of food followed by convulsions		convulsions triggered by the sight of food		Head nodding		Head nodding	
qPCR data		qPCR		qPCR		qPCR		qPCR		qPCR
	Cerebellum cortex	+	Cerebellum cortex	+	Choroid plexus	+	Nervus opticus	-	Nervus opticus	-
	Nucleus dentatus	+	Cerebellum vermis	+	Olfactory nerve	+	Hippocampus	-	olfactory nerve	-
	Frontal cortex	-	Nervus opticus 2	+	Pons	-	Frontal base	-	Pons	-
	Hippocampus	-	Olphactory bulb	+	Nervus opticus	-	Pons	-	Medulla elongata	-
	Choroid plexus	-	Nucleus dentatus	-	Cerebellum vermis	-	choroid plexus	-	Vermis	-
	Olfactory bulb	-	Pons	-	Frontal cortex	-	Vermis	-	choroid plexus	-
	Pons	-	Frontal cortex	-	Thalamus + corpus mamillaria	-	Nucleus dentatus and cortex	-	Frontal cortex	-
			Hippocampus 1	-	Hippocampus	-	Frontal cortex	-	hippocampus	-
			Hippocampus 2	-					hypothalamus left	-
			Choroid plexus	-						
			Nervus opticus	-						
Histological findings			Right corpus mamillaria	-						
Loss Purkunje cells	++		+		+++		+		+++	
Hyperplasia Bergmann glia	+								+	
Loss of neurons	+		+		+				+	
Lymphocytes in meninges	+		+		+					
Cerebellum atrophy	+		+		+		+		+++	
Additional information	ependymitis granularis				generalized spongeosis; Burkitt lymphoma		Severe autolysis		focus of astrocytosis in hypothalamus	

# 25 year follow up study of 295.909 persons with onchocerciasis

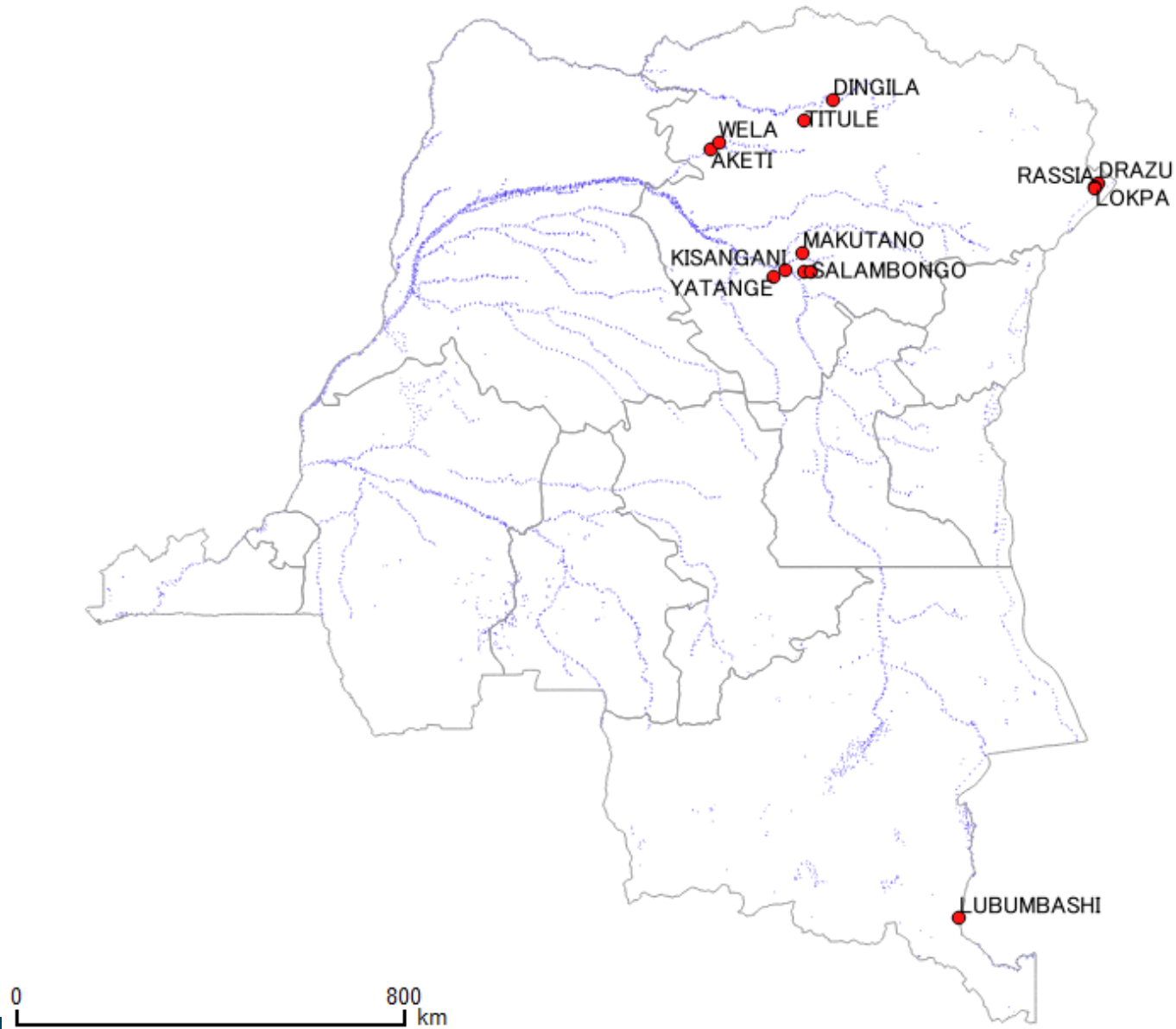
Walker M Plos Negl Trop Dis, 2012 Mar 6(3) e 1578

Onchocerciasis  
kills young  
people: why?



# Democratic Republic of the Congo

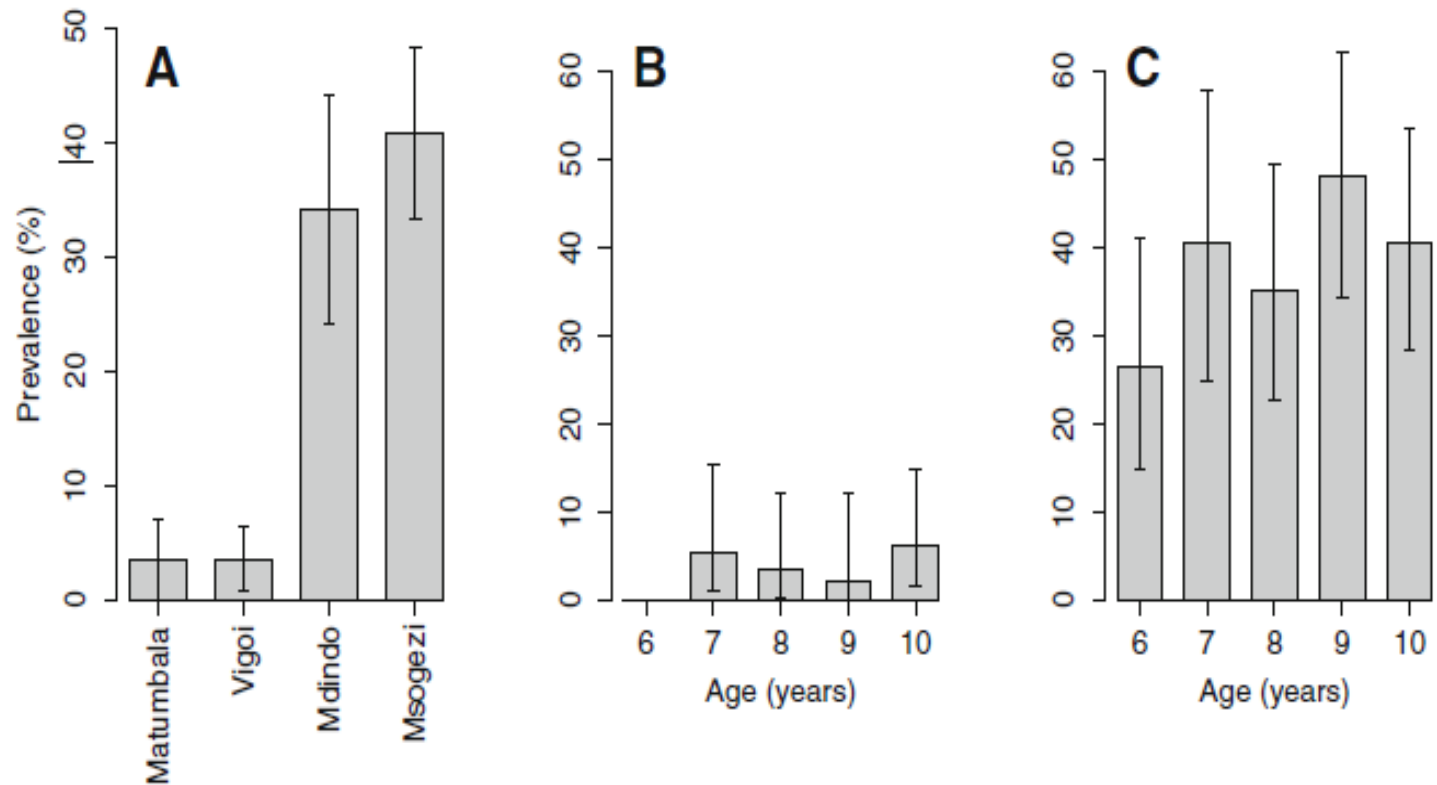
## Study sites



# Prevalence of NS and other forms of epilepsy in villages in northern Uganda

District	Total Population	Prevalence of All cases of Epilepsy & NS combined	Prevalence of NS & NS with other forms of seizures	Prevalence of Other forms of epilepsy
Kitgum	871	79 (9.1%)	36 (4.1%)	43 (4.9%)
Pader	307	29 (9.4%)	15 (4.9%)	14 (4.6%)
Moyo	960	38 (4.0%)	0 (0.0%)	38 (4.0%)
<b>Total</b>	<b>2,138</b>	<b>146 (6.8%)</b>	<b>51 (2.4%)</b>	<b>95 (4.4%)</b>

# OV16 results in Mahenge area, Tanzania



# 'International Workshop on Onchocerciasis-Associated Epilepsy' (OAE 2017)

(12-14 October, University of Antwerp)



With the support of  
THE BELGIAN  
DEVELOPMENT COOPERATION **.be**



# Ituri, case control study: association epilepsy and onchocerciasis

	Persons with epilepsy		Controls	
	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%