



Universiteit  
Antwerpen



# Onchocerciasis-associated epilepsy (OAE) in Mahenge, Tanzania

*PhD Thesis publicly defended by :*

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*19th September, 2023*

*Antwerp, BE*



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University of Antwerp

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# Introduction



# Onchocerciasis

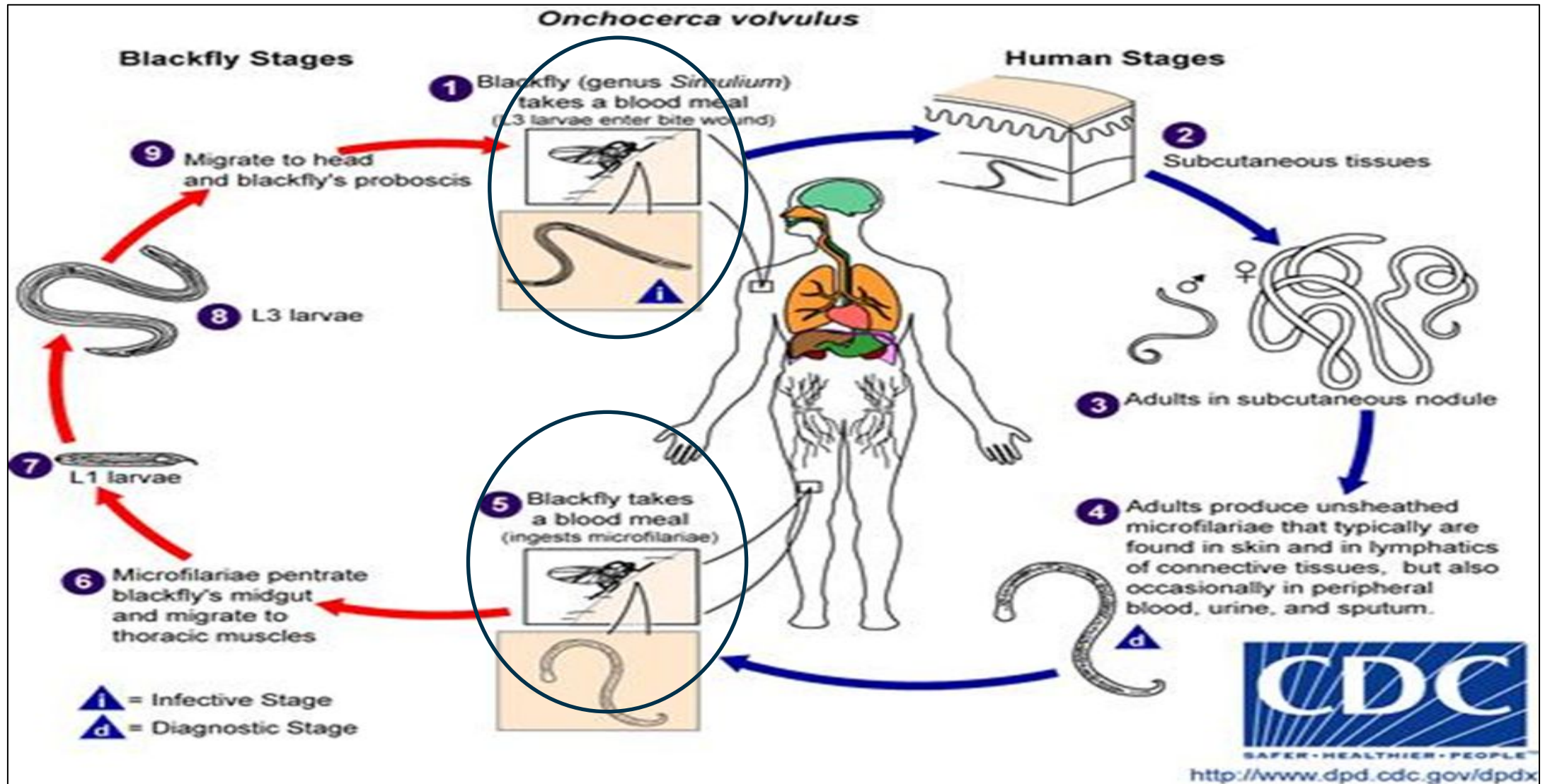
- Onchocerciasis is a parasitic disease caused by the filarial nematode *Onchocerca volvulus* transmitted by blackflies breeding in rapid flowing rivers



- Estimated 21 million people are infected worldwide, 99% in SSA.
- Adult worms in nodules can live for up to 15 years
  - 1,000 microfilariae (mf) released daily
  - Number of mf per person: up to 150 million
  - Mf live for 2 years



# Onchocerciasis life cycle



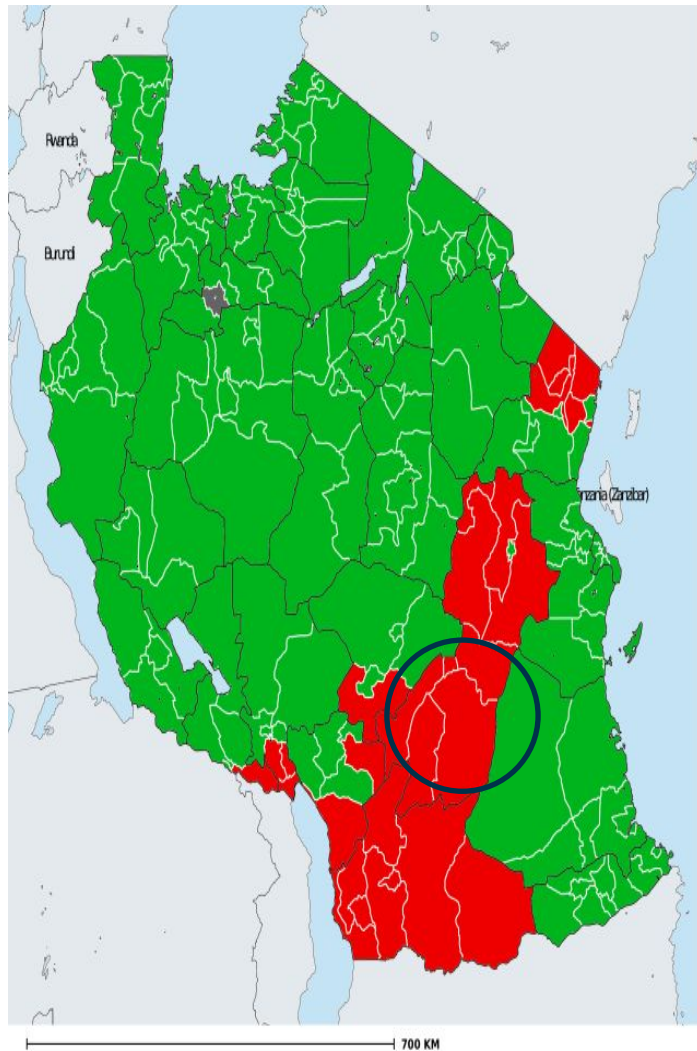
# Onchocerciasis control

- Control of onchocerciasis is by community directed treatment with ivermectin (CDTI)
  - Ivermectin kills the microfilaria, but not the adult worm



- WHO enlisted Onchocerciasis as a priority disease targeted for elimination by 2030.

# Onchocerciasis in Tanzania



## Tanzania (Mainland) (2020)

### Status of Onchocerciasis Elimination

#### Onchocerciasis > Endemicity

- Not suitable for Onchocerciasis
- Endemic (requiring MDA)
- Unknown (under LF MDA)
- Under post-intervention surveillance
- Unknown (consider Oncho Elimination Mapping)
- No data available

Boundaries, names and designations used here do not imply expression of WHO opinion concerning the legal status of any country, territory or area, or of its authorities, or concerning delimitation of frontiers or boundaries. Dotted / dashed lines represent approximate border lines for which there may not yet be full agreement.

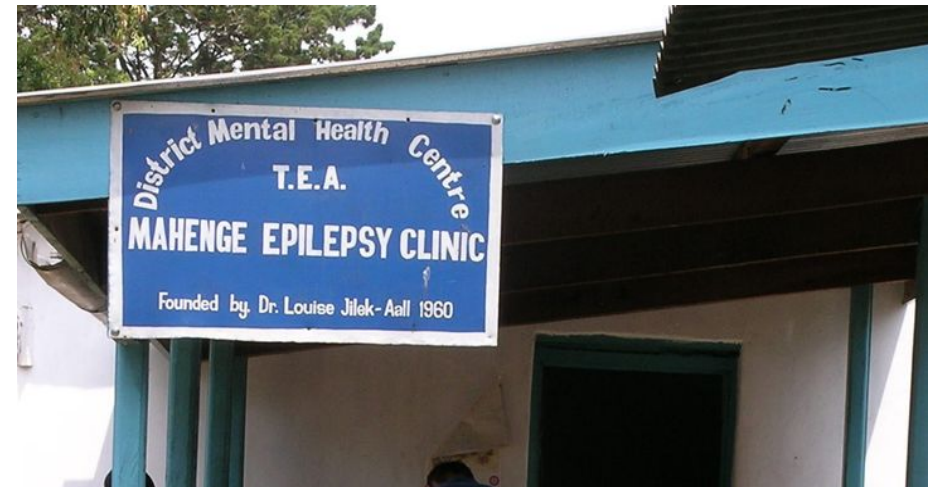
**Data Source:**  
Data provided by health ministries to ESPEN through WHO reporting processes. All reasonable precautions have been taken to verify this information  
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- Eight foci in Tanzania are endemic for onchocerciasis
- 7.2 million (3% of 240 million global population) at risk
- The Mahenge focus was historically one of the most heavily infected foci
  - 87% infection in certain communities

# Epilepsy

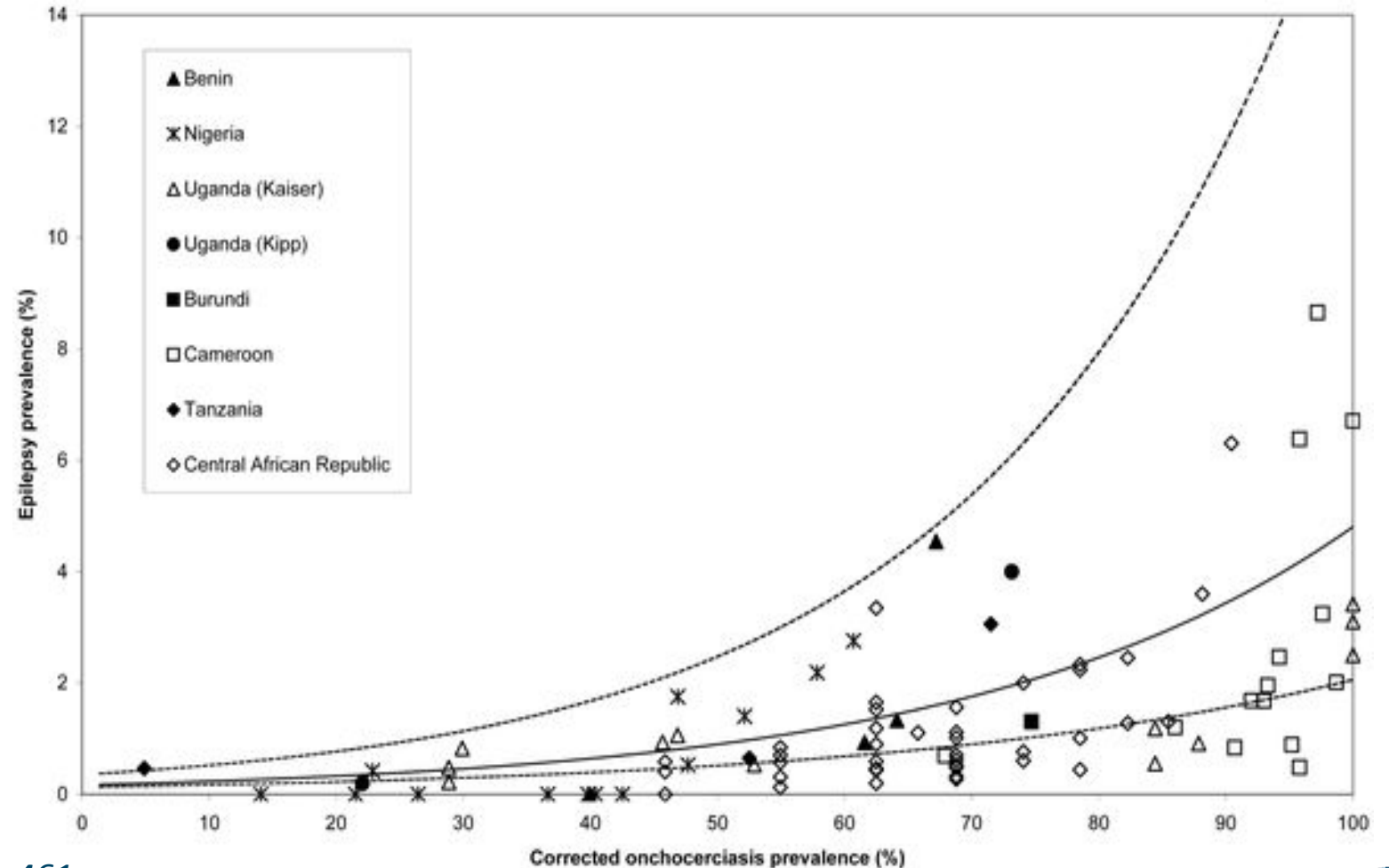
- Epilepsy the most common neurological disease
- 50M people are estimated to be affected by epilepsy globally, of them 80% lives in LMICs.
- Several parasitic infections
  - Severe malaria
  - Neurocysticercosis
  - Onchocerciasis
- Mahenge area is one of the area with the highest epilepsy prevalence in Tanzania



# Onchocerciasis-associated epilepsy (OAE)

## Meta-analyses investigating the association between onchocerciasis and epilepsy

- There on average a 0.4% increase in epilepsy prevalence for each 10% increase in onchocerciasis prevalence





# OAE case definition for epidemiological purposes

## Minimal criteria

1. A history of two or more unprovoked epileptic seizures occurring at least 24 h apart
2. Living in an onchocerciasis-endemic region for at least three years
3. Living in a village with a high prevalence of epilepsy and PWE often clustered within certain households, that is, families having more than one child with epilepsy
4. No other obvious cause of epilepsy (e.g., perinatal asphyxia, history of severe malaria, measles, encephalitis or meningitis, or head injury with loss of consciousness in the five years before the onset of epileptic seizures)
5. Onset of seizures in childhood or adolescence (3 to 18 years)
6. Normal neurological development before the onset of epilepsy

*Van Cutsem G et al. . Case definitions for onchocerciasis-associated epilepsy and nodding syndrome: A focused review. Seizure. april 2023*

# Pathogenesis of OAE

## Hypothesis

- Epilepsy is induced by *O. volvulus* mf that occasionally may penetrate the brain in children with high mf load.
  - Mf were detected in the cerebrospinal fluid (CSF)
    - Hissette (1932) DRC
    - Mazotti (1959 in Mexico) and in
    - 1976 by Duke in Cameroon
- Since CDTI, *O. volvulus* mf nor DNA could be detected in the CSF nor in the brain during post-mortem studies
- However, CSF was collected in persons many years after the onset of the seizures and the *O. volvulus* DNA may have been eliminated by the immune system (macrophages, microglia cells)

# Pathogenesis of OAE

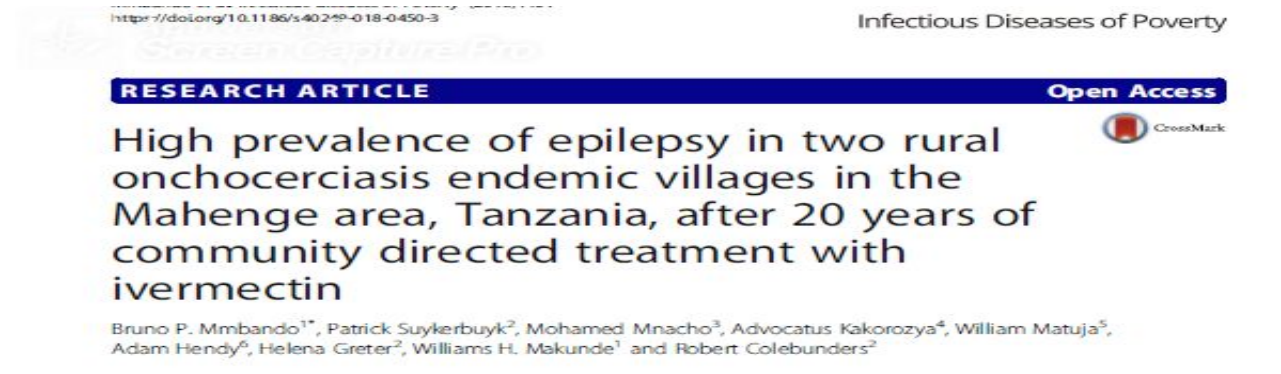
## Other hypothesis

- Autoimmune disorder induced by neurotoxic Leiomodin-1 antibodies cross reacting with *O. volvulus*?
  - Hypothesis not confirmed
- Tau deposits also observed in Alzheimer disease, were detected in the brain of persons with OAE
  - Tau deposits more likely to be the consequence of the disease, because of repetitive seizures, inflammation *O. volvulus* induced directly or indirectly?

# Thesis rationale

## Epilepsy and Onchocerciasis situation in Mahenge in 2018

- High prevalence of epilepsy
  - >3% in rural villages
- High transmission of onchocerciasis
  - >40% OV16 prevalence, children 6-11yrs in rural setting
- Reasons for persistence of onchocerciasis transmission despite > 20 years of annual CDTI
  - Could it be due to poor response to ivermectin/resistance?



# Thesis rationale

## Community interventions

- A community based epilepsy treatment program
- Increase ivermectin coverage by switching from annual to bi-annual (6 monthly) CDTI

# Main objective

To determine the burden of disease caused by onchocerciasis associated epilepsy (OAE)



To investigate interventions to decrease the OAE burden of disease

# Studies: mixed methods

## To investigate the burden of OAE disease

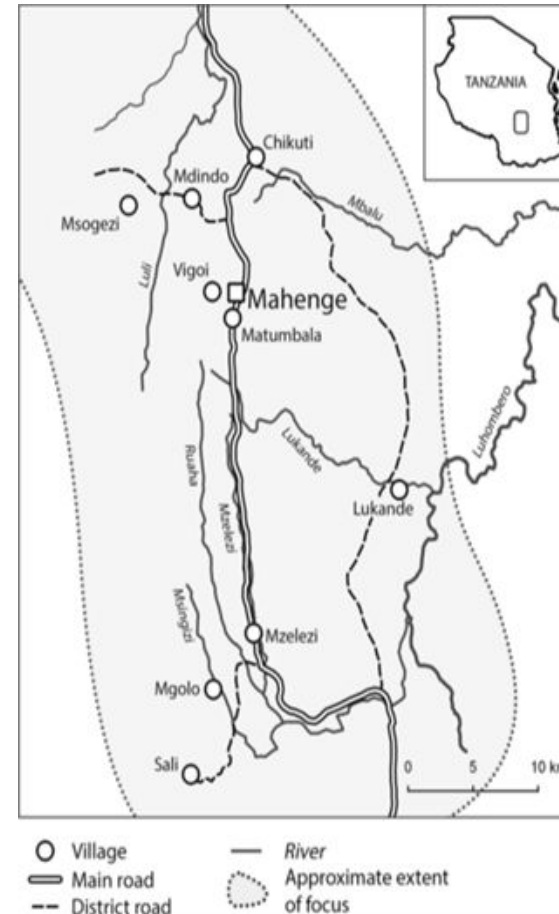
1. Describe the clinical characteristics and the prevalence OAE in Mahenge
2. Assess community knowledge, attitudes, and practices regarding epilepsy in Mahenge

## To evaluate interventions to decrease the OAE burden

3. Impact of peer support groups in reducing epilepsy related stigma
- Reasons for persistent onchocerciasis transmission despite 20 years of CDTI
  4. Ivermectin treatment response
  5. Ivermectin uptake
6. The effect of bi-annual CDTI on the incidence of OAE

# Study site

- Mahenge area of Ulanga district
  - Urban villages: Matumbala, Vigoi,
  - Rural villages Mdindo, Msogezi, Mzelezi and Sali
- Mountainous topography with fast flowing rivers and streams
- High endemicity of onchocerciasis since the early last century
- CDTi was introduced in the Mahenge area in 1997





# Study 1: To describe the clinical characteristics and the prevalence OAE in Mahenge

› [Epileptic Disord.](#) 2019 Oct 1;21(5):425-435. doi: 10.1684/epd.2019.1093.

## **Clinical presentation of epilepsy in six villages in an onchocerciasis endemic area in Mahenge, Tanzania**

Dan Bhwana <sup>1</sup>, Bruno P Mmbando <sup>1</sup>, Marieke Cj Dekker <sup>2</sup>, Mohamed Mnacho <sup>3</sup>,  
Advocatus Kakorozya <sup>4</sup>, William Matuja <sup>3</sup>, Williams H Makunde <sup>1</sup>, Sarah Weckhuysen <sup>5</sup>,  
Robert Colebunders <sup>6</sup>

# Methods

- Community based cross-sectional study:
  - In four rural and two sub-urban villages in 2017 and 2018
  - Enumeration of the village population
  - Identify individuals suspected to have epilepsy by asking 5 validated questions
  - Confirmation of epilepsy diagnosis by an neurologist or trained medical officer
  - Suspected individuals were tested for OV16 antibodies



# Clinical presentation of epilepsy

Strata	Village	Number screened	No. PWE (%)	Sex of PWE Male (%)	Median age of PWE (IQR)	Median age of onset of epilepsy (IQR)
Sub-urban	Matumbala	972	16 (1.6)	7 (43.7)	31.5 (18.9–43.2)	13 (5–18)
	Vigoi	1646	23 (1.4)	12 (52.2)	23.7 (17.5–31.5)	10 (7–14)
Rural	Sali	1176	43 (3.7)	14 (38.9)	21.4 (15.6–29.6)	10 (6–12)
	Mzelezi	1769	51 (2.9)	24 (51.1)	22.6 (17.6–25.6)	12 (6–19)
	Mdindo	941	33 (3.5)	17 (51.5)	27.5 (22.5–36.5)	12 (11–15)
	Msogezi	1558	55 (3.5)	26 (47.3)	25.5 (17.5–33.5)	10 (6–16)

*PWE=number of persons with epilepsy; IQR: interquartile range.*

- Nodding seizures were reported in 12.7% of PWE
- PWE from the rural areas were 88.2% OV16 positive compared to 75.3% in urban area 75.3%;  $p=0.021$
- 77.9% of PWE met the criteria of the clinical case definition of OAE

# Clinical presentation of PWE

	Nodding seizures (n=31)	Other forms of epilepsy (n=190)	p-value
Age (median, IQR)	22.50 (17–26)	23.69 (19–34)	0.355
Sex (males)	16 (53.3)	85 (47.0)	0.518
Positive Ov16 test	21 (70%)	81 (52.6%)	0.064
Seizure in week preceding the survey	16 (51.6)	46 (24.3)	0.002
Psychiatric symptoms*	12 (38.7)	40 (21.05)	0.032
Nakalanga features	9 (29.0)	15 (8.0)	<0.001
Intellectually disabled	16 (51.6)	45 (23.9)	0.001
Normal gait	26 (83.9)	178 (93.9)	0.057
Taking anti-epileptic drugs	26 (83.9)	112 (59.0)	0.008
Regular use of AEDs (good adherence)**	14 (45.2)	78 (44.8)	0.97

# Nakalanga features



A 23 year old male with Nakalanga features and his relative of the same age without abnormal features.

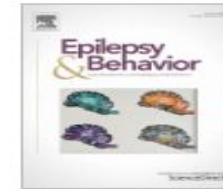
# Conclusion

- There was a higher epilepsy prevalence in the rural than sub-urban villages
- The high epilepsy prevalence in rural villages is related to the high prevalence of OAE
- Nodding syndrome is associated with more disabilities than persons with other forms of OAE

## Study 2: To assess community knowledge, attitudes and practices regarding epilepsy in Mahenge



Epilepsy & Behavior  
Volume 128, March 2022, 108568

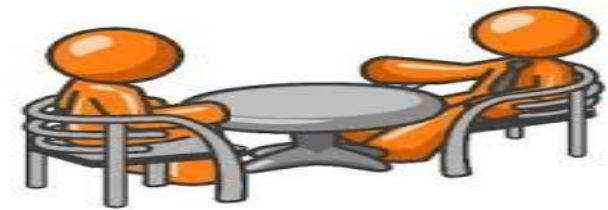


Community knowledge, attitudes, and practices regarding epilepsy in Mahenge, Tanzania: A socio-anthropological study in an onchocerciasis-endemic area with a high prevalence of epilepsy

Bruno P. Mmbando<sup>a</sup>  , Dan K. Bhwana<sup>a</sup>, Isolide S. Massawe<sup>a</sup>, Pendo Magili<sup>a</sup>, Sloan Mahone<sup>b</sup>, Williams Makunde<sup>a</sup>, Adiel K. Mushi<sup>c</sup>, Robert Colebunders<sup>d</sup>

# Methods

- Qualitative study conducted in June and July 2019
- Eleven focus group discussions with PWE & their care takers, Community-Directed Distributors (CDDs) and Community resource persons (CORPs)
- Two in-depth interviews (IDIs) with district and zonal NTD program coordinators
- Data was analysed manually using content analysis





## Knowledge about epilepsy

Epilepsy was well known by all groups

*“The biggest disease that bothers us in our village is epilepsy. We do not know what causes this disease. Malaria is also another disease that afflicts us”*

*[Sali: Male PWE Caretakers]*

## Association between epilepsy and onchocerciasis

*"To my knowledge, it is possible that onchocerciasis is a major cause of this disease; experience from the past when ivermectin was introduced show that the epilepsy cases have been declining and even the skin rashes have now disappeared. My belief is that the parasite goes directly into the human brain and then causes epilepsy"*

*[Sali: CORP 09]*

## Seeking care among people with epilepsy

*“To my knowledge, all people from this village who suffer from epilepsy are taken to traditional healers first”*

*[Sali: CORP 4]*

# Conclusion

- Epilepsy presents a major burden for PWE and their close relatives in the Mahenge area.
- Traditional healers are the first contact during health seeking epilepsy treatment and thus delays seeking treatment at the health facilities

# Study 3: To determine the impact of peer support group intervention to decrease epilepsy-related stigma in Mahenge

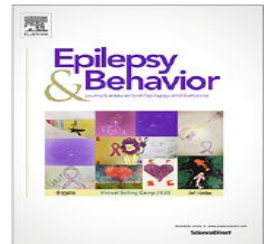
Epilepsy & Behavior 124 (2021) 108372



Contents lists available at [ScienceDirect](#)

## Epilepsy & Behavior

journal homepage: [www.elsevier.com/locate/yebeh](http://www.elsevier.com/locate/yebeh)



### A peer support group intervention to decrease epilepsy-related stigma in an onchocerciasis-endemic area in Mahenge, Tanzania: A pilot study

Dan Bhwana<sup>a,b</sup>, Lies Das<sup>b</sup>, Joseph Nelson Siewe Fodjo<sup>b</sup>, Filbert Francis<sup>a</sup>, Daniel P. Challe<sup>a</sup>, Holmes W. Makunde<sup>a</sup>, Bruno P. Mmbando<sup>a</sup>, Robert Colebunders<sup>b,\*</sup>

<sup>a</sup> National Institute for Medical Research, Tanga Research Centre, Tanga, Tanzania

<sup>b</sup> Global Health Institute, University of Antwerp, Antwerp, Belgium



# Methods

- A community-based epilepsy program was established in 4 rural villages
- In 2 of them (Mdindo and Sali) a peer support group (PSG) was established involved PWE and their caregivers
- PSG aimed to bring PWE and their families together during monthly meetings to discuss epilepsy-related issues
- Perceived stigma was measured using the validated Kilifi stigma scale of epilepsy



# Multivariate model investigating predictors of stigma score

Model* covariates	Adjusted Regression Coefficient [95% Confidence Interval]	P-value
Peer support group	-0.120 [-1.580, 2.816]	0.872
Age (in years)	0.021 [-0.054, 0.097]	0.582
Male gender	0.513 [-0.920, 1.947]	0.484
Is married	-0.456 [-2.498, 1.585]	0.662
<b>Has attended school</b>	<b>1.821 [0.345, 3.297]</b>	<b>0.017</b>
Duration of epilepsy	0.003 [-0.096, 0.102]	0.952
History of nodding seizures (past or present)	0.121 [-1.532, 1.774]	0.886
<b>Number of seizures during the preceding week</b>	<b>1.013 [0.568, 1.457]</b>	<b>&lt; 0.001</b>
History of sexual abuse	2.246 [-1.241, 5.734]	0.209
<b>History of physical abuse</b>	<b>3.200 [0.574, 5.827]</b>	<b>0.018</b>
<b>Random effects (clustering variable: Village)</b>		
Variance of the variable "village"	0	
Residual variance	4.072	
Number of groups	4	

\*Adjusted R-squared: 0.259

## Conclusion

- Perceived epilepsy-related stigma in Mahenge is still a major public health problem
- The peer support group intervention did not reduce the stigma
- Insufficient accompaniment provided to peer support members?
- Reducing seizures frequency may reduce epilepsy-related stigma?



# Study 4: To investigate the reasons for persistent onchocerciasis transmission despite of 20 years of ivermectin distribution: **ivermectin treatment response**



**African Health Sciences**

Makerere Medical School

[Afr Health Sci](#). 2022 Sep; 22(3): 607–616.

doi: [10.4314/ahs.v22i3.65](https://doi.org/10.4314/ahs.v22i3.65)

PMCID: PMC9993262

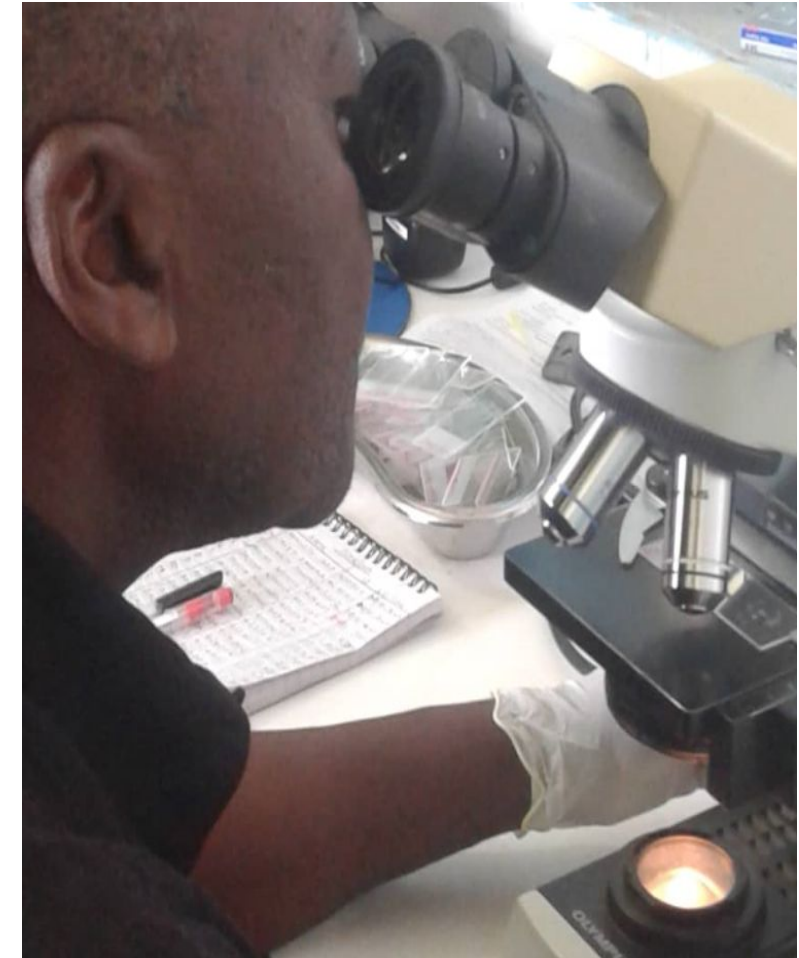
PMID: [36910370](https://pubmed.ncbi.nlm.nih.gov/36910370/)

**Ivermectin treatment response in two rural villages with a high prevalence of onchocerciasis and epilepsy, Mahenge Tanzania**

[Dan Bhwana](#),<sup>1,2</sup> [Bruno P Mmbando](#),<sup>1</sup> [Alfred Dusabimana](#),<sup>2</sup> [Athanas Mhina](#),<sup>1</sup> [Daniel P Challe](#),<sup>1</sup> [Joseph N Siewe Fodjo](#),<sup>2</sup> [Williams H Makunde](#),<sup>1</sup> and [Robert Colebunders](#)<sup>2</sup>

# Methods

- April - September 2019
- 50 PWE and 160 randomly selected persons without epilepsy from Msogezi and Mdindo villages in Mahenge participated in a follow-up study
- Skin snips were obtained pre- and three months post-ivermectin treatment
- Key outcome:  $\geq 80\%$  microfilaria reduction



# Results

- Overall *O. volvulus* positive skin snip prevalence at baseline was 49% (103/210)
  - People with epilepsy (58.0%)
  - People without epilepsy (46.3%)
- 76/163 (46.6%) individuals with positive skin snips with pre- and a post-ivermectin skin snip result Vs 29/163 (17.8%) post IVM,  $p < 0.001$
- 54 (81.8%, 95%CI:72.3-91.4) of them had a microfilarial density reduction of  $\geq 80\%$



..\data\pictures\Oncho\_filarial\_slide  
Trim.mp4

# Results

## Factors associated with mf density three months post ivermectin use

Covariates	Univariate		Multivariate	
	IR (95%CI)	P-value	IR (95%CI)	P-value
Sex (Female)	0.72 (.26 - 1.98)	0.528		
Age (in years)	1.01 (0.99 - 1.04)	0.233		
Being a PWE	0.997 (0.34 - 2.97)	0.996		
Village of residence: Msogezi	0.34 (0.12 - 0.91)	0.032	0.577 (0.20-1.67)	0.310
BMI – Underweight (< 18.5)	0.50 (0.18 - 1.38)	0.180		
<b>Pre-ivermectin mf density*</b>	<b>1.77 (1.27-2.46)</b>	<b>0.001</b>	<b>1.65 (1.18 - 2.31)</b>	<b>0.003</b>

*\*Log-transformed*



# Conclusion

- Satisfactory decrease in microfilarial density following ivermectin treatment in most individuals.
  - Ivermectin is effective in control of onchocerciasis
- Optimizing ivermectin coverage will address the on-going onchocerciasis transmission in Mahenge



# Study 5: To investigate the reasons for persistent onchocerciasis transmission despite of 20 years of ivermectin distribution: **ivermectin uptake**

ORIGINAL RESEARCH article

Front. Trop. Dis, 03 April 2023

Sec. Neglected Tropical Diseases

Volume 4 - 2023 | <https://doi.org/10.3389/fitd.2023.1079012>

## Factors associated with low-uptake of ivermectin in Mahenge, an area with high prevalence of onchocerciasis and epilepsy in Tanzania: A qualitative perspective



Dan Bhwana<sup>1\*</sup>



Isolide S. Massawe<sup>1</sup>



Adiel K. Mushi<sup>2</sup>



Pendo Magili<sup>1</sup>



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Williams Makunde<sup>1</sup>



Bruno P. Mmbando<sup>1</sup>



Robert Colebunders<sup>3</sup>

## General knowledge and disease burden

Onchocerciasis was well known by all participants from all groups with different local terminologies used to describe the disease, such as

- “*ukurutu/mkita*” (itching and dry skin)
- “*lung’ang’a*” (leopard skin, the chronic skin pigmentation caused by onchocerciasis).



## Perceived reasons for not taking ivermectin

*“We cannot swallow these medications since they reduce sexual drive in men and at the end, we will not be able to reproduce, ..., You cannot find these medications in town even white people do not use them”*

*[Sali, CORP]*



## Perceived challenges during mass drug administration

*“Some households are located too far from the village, and it is difficult to reach them repeatedly, especially when distributing ivermectin; you can go around even three times without finding residents”*

*[Mzelezi, CDD]*

# Conclusion

- Misconceptions concerning side effects of ivermectin need to be addressed
- Continuous advocacy is needed to take ivermectin bi-annually and the supervision of the CDDs during CDTI need to be improved
- The number of CDTI days need to be increased particularly in hard to reach areas

# Study 6. To evaluate the effect of a bi-annual community directed treatment with ivermectin strategy on transmission and incidence of OAE

## PLOS NEGLECTED TROPICAL DISEASES

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### RESEARCH ARTICLE

# Impact of a bi-annual community-directed treatment with ivermectin programme on the incidence of epilepsy in an onchocerciasis-endemic area of Mahenge, Tanzania: A population-based prospective study

Dan Bhwana<sup>1</sup>✉, Luís-Jorge Amaral<sup>2</sup>✉, Athanas Mhina<sup>1</sup>, Paul Martine Hayuma<sup>1</sup>, Filbert Francis<sup>1</sup>, Joseph N. Siewe Fodjo<sup>2</sup>, Bruno P. Mmbando<sup>1</sup>, Robert Colebunders<sup>2</sup>✉\*

# Methods

- Door-to-door epilepsy survey in 2017 (Mdindo and Msogezi) and in 2018 (Mzelezi and Sali)
- Door-to-door epilepsy survey in August 2021
- Number of new epilepsy cases for a given year was determined by asking the age of onset of the seizures
- Incidence rate =  
$$\frac{\text{New epilepsy cases in 3 years before the survey}}{\text{Total population surveyed} \times 3}$$



# Results

## Bi-annual CDTi coverage in 2021 overall and per round.

Village		Mdindo	Msogezi	Mzelezi	Sali	Overall
<b>CDTi coverage<sup>A</sup></b> n/T % (95%CI)	<b>1<sup>st</sup> round</b> (March 2021)	619/793 78.1 (75.0-80.9)	1564/1926 81.2 (79.4-82.9)	1843/2233 82.1 (80.4-83.7)	1129/1371 82.4 (80.2-84.3)	5146/6314 81.5 (80.5-82.5)
	<b>2<sup>nd</sup> round</b> (August 2021)	615/792 77.7 (74.6-80.5)	1488/1925 77.3 (75.3-79.1)	1779/2224 80.0 (78.3-81.6)	964/1367 70.5 (68.0-72.9)	4846/6308 76.8 (75.8-77.9)
	<b>Total<sup>B</sup></b> (2021)	632/796 79.4 (76.4-82.1)	1585/1932 82.0 (80.2-83.7)	1854/2228 83.2 (81.6-84.7)	1137/1372 82.9 (80.7-84.8)	5208/6328 <b>82.3 (81.3-83.2)</b>

<sup>A</sup> Two hundred and seventy people did not provide information about their ivermectin intake and were excluded from the population to calculate the CDTi coverage.

<sup>B</sup> Persons who took ivermectin in one or both CDTi rounds in 2021.

# Results

## Incidence of overall epilepsy and of probable nodding syndrome pre- and post-bi-annual CDTi in four rural villages

Surveys	Pre-intervention incidence (2015/16-2017/18)* (data obtained during the 2017/18 surveys)*				Post-intervention incidence (2019-2021) (data obtained during the 2021 survey)			
	Overall epilepsy incidence		pNS incidence		Overall epilepsy incidence		pNS incidence	
	n	n/100,000 (95%CI) PY	n	n/100,000 (95%CI) PY	n	n/100,000 (95%CI) PY	n	n/100,000 (95%CI) PY
<b>Mdindo</b>	4	141.7 (45.4-389.0)	1	35.4 (1.9-229.8)	0	0.0 (0.0-187.8)	0	0.0 (0.0-187.8)
<b>Msogezi</b>	8	171.2 (79.6-351.5)	1	21.4 (1.1-138.8)	2	33.3 (5.8-134.3)	0	0.0 (0.0-79.7)
<b>Mzelezi</b>	12	226.1 (122.6-406.8)	1	18.8 (1.0-122.3)	6	86.5 (35.2-198.5)	1	14.4 (0.8-93.6)
<b>Sali</b>	5	141.7 (52.2-351.1)	0	0.0 (0.0-111.2)	1	23.2 (1.2-150.7)	0	0.0 (0.0 – 111.2)
<b>Overall</b>	29	<b>177.6 (121.2-258.5)</b>	3	<b>18.4 (4.7-58.5)</b>	9	<b>45.5 (22.2-89.7)</b>	1	<b>5.1 (0.3-32.8)</b>

Eight of the new epilepsy cases 2019-21 did not take ivermectin in the year they developed seizures

## Conclusion

- A bi-annual CDTi programme should be preferred to eliminate onchocerciasis in areas with high prevalence of onchocerciasis and epilepsy
- High CDTi coverage among children is particularly important to prevent OAE

# Overall conclusions

- OAE is an important public health problem in areas with high onchocerciasis transmission and a sub-optimal onchocerciasis elimination program
- OAE presents with a spectrum of epileptic seizures
- NS is a form of OAE associated with a high degree of disability
- OAE is a preventable condition by strengthening the onchocerciasis elimination program



# Research recommendations

- Research is needed to optimize onchocerciasis elimination programs in onchocerciasis endemic areas with a high prevalence of OAE
- Research is needed to evaluate innovative interventions to decrease epilepsy related stigma
- Research is needed to identify the pathogenesis of OAE

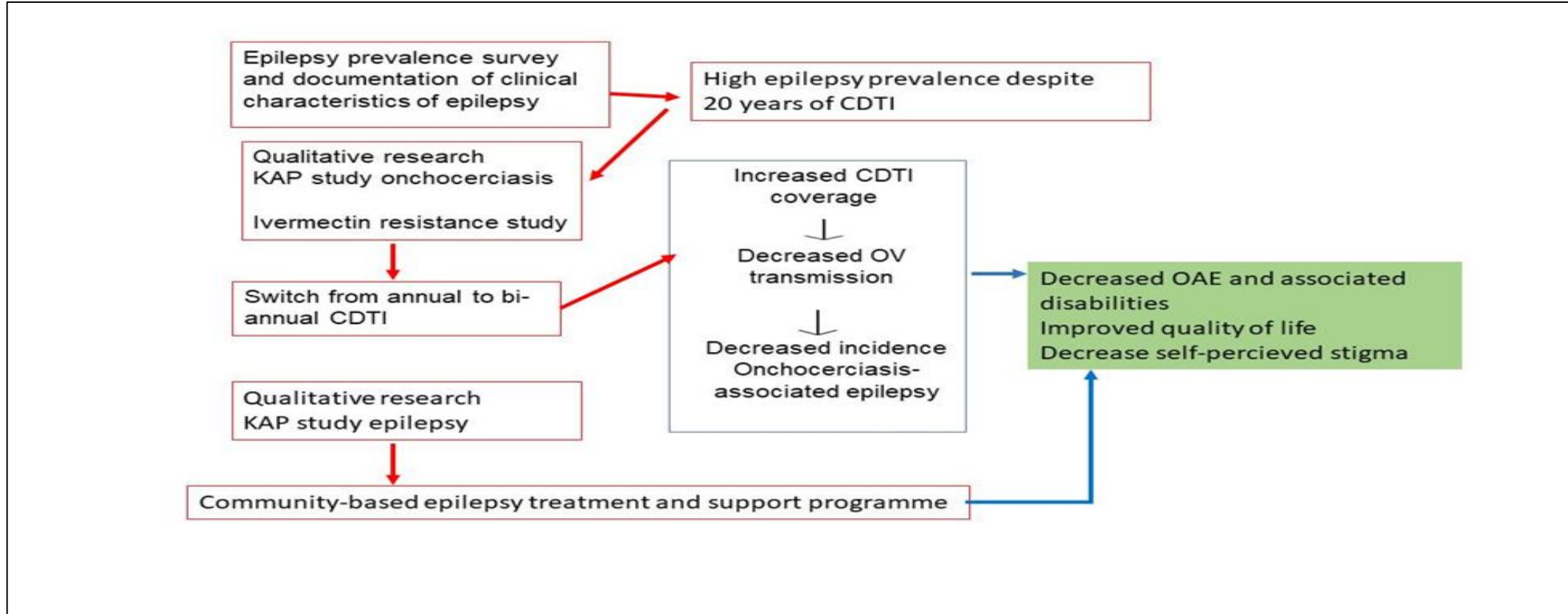
# Acknowledgements

**Tanzania team:** B.P. Mmbando, W. Makunde, I. Massawe, D. Challe, G. Nkya, B. Swai, P. Faustine, A. Mushi, A. Mhina, M. Chiduo, V. Baraka, M. Mnacho, W. Matuja

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# Ultimate goal of the PhD work



*Linkage between studies and ultimate goal of the PhD work*

# Clinical characteristics of PWE according to OV16 status

	<b>OV16 positive</b> <i>n</i> =102 (54.5%)	<b>OV16 negative</b> <i>n</i> =85 (45.5%)	<b><i>P</i>-value</b>
Gender-Male, <i>n</i> (%)	46 (46.9)	39 (47.6)	0.934
Age, (median, IQR)	25.4 (18.6–37.5)	22.6 (16.13-31.7)	0.048
Age of onset of epilepsy, (mean ± SD)	14.1 ± 9.6	12.3 ± 7.7	0.172
<b>Nodding seizures, <i>n</i> (%)</b>	<b>21 (20.6)</b>	<b>9 (10.16)</b>	<b>0.064</b>
Psychiatric symptoms, <i>n</i> (%)	27 (26.5)	17 (20.0)	0.30
<b>Setting (rural vs. urban), <i>n</i> (%)</b>	<b>90 (88.2)</b>	<b>64 (75.3)</b>	<b>0.021</b>