



# Epidemiology of Epilepsy in Africa and relevance to Onchocerciasis

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# Outline

- ILAE Classification of Epilepsy
  - Seizures
    - Convulsive vs Non-convulsive
  - Syndromes
  - Aetiology
- Epidemiological parameters
  - Incidence – Prevalence – Spontaneous remission – Mortality
  - Incidence
    - Recall vs Ongoing surveillance
  - Population attributable fraction

# Epidemiology, causes, and treatment of epilepsy in sub-Saharan Africa

Awa Ba-Diop, Benoît Marin, Michel Druet-Cabanac, Edgard B Ngougou, Charles R Newton, Pierre-Marie Preux

Lancet Neurology 2014

- Prevalence of lifetime epilepsy in SSA:
  - Median 14.2 per 1000
  - Compared to
    - 4–8/1000 in West
    - 6/1000 in Asia
- But wide range in prevalence estimates:
  - 2 -105/1000
- ? Causes
  - Real differences
  - Methodological
    - Case detection:
      - Community screens most reliable
    - Case definition
    - Investigations
- Studies detected mainly convulsive epilepsies

	Year	N	Prevalence, per 1000 (95% CI)	Sex ratio (M/F)	Proportion aged <20 years	Method	Population
<b>West Africa</b>							
Benin*	2012	13 046	8.0 (6.59–9.74)	0.7	18.1%	DTD	Rural
Benin*	2007	1232	10.6 (5.9–18.5)	NA	NA	CS	Urban
Benin (Cotonou)*	2003	1400	7.9 (4.5–14.5)	1.6	82.0%	CS	Urban
Benin (Dangbo)**	2007	737	31.0 (18.4–43.5)	0.8	45.7%	CS	Rural
Benin (Zirrie)**	2000	3134	15.9 (12.3–24.3)	0.8	52.4%	DTD	Rural
Burkina Faso*	1993	16 627	10.6 (9.3–12.2)	1.7	76.2%	CS	Rural
Burkina Faso*	2012	888	45.0 (33.0–60.0)	NA	NA	CS	Rural
The Gambia*	2002	16 200	8.9 (4.5–5.3)	NA	NA	DTD	Rural
Ghana (Kintampo)*	2013	129 812	4.9 (4.4–5.3)	0.8	NA	DTD	Rural
Côte d'Ivoire*	1988	1176	7.6 (2.6–12.6)	0.7	88.8%	CS	Rural
Côte d'Ivoire*	1995	920	59.0 (43.7–74.2)	1.4	36.4%	CS	Rural
Côte d'Ivoire*	1990	309	78.4 (49.0–104.9)	0.5	91.3%	CS	Rural
Liberia*	1983	4436	28.0 (23.1–32.8)	1.1	NA	CS	Rural
Niul*	2000	5243	13.3 (10.5–16.7)	0.1	NA	DTD	Rural
Nigeria*	1989	2925	6.2 (3.4–9.0)	0.1	61.5%	CS	Rural
Nigeria (Aiyé)**	1982	903	37.0 (24.7–49.3)	0.6	NA	CS	Rural
Nigeria (Igbu-Ora)**	1987	18 954	5.3 (4.2–6.3)	0.9	NA	CS	Urban
Senegal*	1986	7682	8.3 (6.2–10.4)	NA	65.6%	CS	Rural
Senegal*	2005	4500	14.2 (10.7–17.7)	NA	39.2%	CS	Urban
Togo (Kozah)**	1989	5264	15.7 (13.2–20.2)	1.6	NA	CS	Rural
Togo (Tona)**	2000	9155	18.6 (15.8–21.3)	0.9	NA	DTD	Rural
Togo (Batambéri)**	2007	6249	15.7 (12.7–19.2)	1.4	29.6%	CS	Rural
<b>East Africa</b>							
Ethiopia**	2006	1154	29.5 (19.7–39.3)	1.1	57.0%	DTD	Rural
Kenya*	1994	7450	4.0 (2.6–5.4)	0.8	50.6%	DTD	Rural
Kenya*	1988	2960	18.2 (13.3–23.0)	NA	NA	DTD	Rural
Kenya (Kisumu)**	2008	10 218	41.0 (31.0–51.0)	1.0	NA	CS	Rural
Kenya (Kisumu)**	2013	233 881	3.8 (3.5–4.0)	1.0	NA	DTD	Rural
Kenya*	2008	151 408	2.9 (2.6–3.2)	1.0	44.2%	DTD	Rural
Tanzania*	2009	7399	13.2 (11.9–14.5)	1.0	59.1%	CS	Rural
Tanzania*	2012	38 523	2.9 (2.4–3.5)	1.0	23.9%	CS	Rural
Tanzania (Haji)**	2012	204 889	2.9 (2.5–3.2)	1.0	NA	CS	Rural
Tanzania (Ifakara)*	2013	204 889	7.2 (6.5–7.8)	1.4	NA	CS	Rural
Tanzania**	2005	4905	7.4 (5.0–9.8)	0.8	NA	DTD	Rural
Tanzania**	1992	18 183	12.1 (10.5–13.7)	0.9	60.8%	CS	Rural
Uganda*	1996	4743	13.0 (9.7–16.2)	NA	NA	DTD	Rural
Uganda*	2010	440	3.0 (1.94–3.20)	1.0	100%	DTD	Rural
Uganda (Iganga-Mayuge)**	2013	69 186	5.0 (4.4–5.6)	1.8	NA	CS	Rural
<b>Central Africa</b>							
Cameroon*	2007	1898	35.4 (27.4–43.4)	1.2	89.2%	DTD	Rural
Cameroon (Killing)**	2008	181	134.5 (90.0–178.0)	1.2	NA	DTD	Rural
Cameroon (Bilomo)**	2000	1900	58.4 (47.8–69.0)	0.9	NA	CS	Rural
Cameroon*	1989	500	70.0 (47.6–92.3)	NA	NA	CS	Rural
<b>Southern Africa</b>							
Madagascar**	2004	925	23.5 (11.6–30.0)	0.5	NA	DTD	Urban
Rwanda*	2008	6757	7.0 (5.0–9.0)	0.8	NA	CS	Rural/urban
South Africa**	2000	6630	7.3 (5.3–9.3)	NA	NA	CS	Rural
South Africa (Agincourt)**	2013	82 818	3.4 (3.0–3.8)	1.0	NA	DTD	Rural
Zambia*	2004	55 000	12.5 (11.6–13.4)	1.3	70.9%	DTD	Rural

DTD=door-to-door; CS=cross-sectional; NA=not available. \*Active epilepsy.

Table 2: Studies of the prevalence of epilepsy in sub-Saharan Africa

# Why Convulsive Epilepsies

- Non-convulsive seizures unreliably detected in Africa

*Newton et al S Afr Med J 1984; 66: 21-23*

- Convulsive epilepsy associated with

- Most stigma
- Morbidity e.g. burns
- Mortality

- Epilepsy

- 2 or more unprovoked seizures in a lifetime

- Active: seizures within the last year

- Used by International League Against Epilepsy  
*Menairdi et al Epilepsia 2001 42(1); 136-8*
- Criteria for starting treatment in the countries

# International League Against Epilepsy (ILAE) Definitions

- Epileptic seizure
  - A transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain
- *Fisher RS et al Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia, 58(4):531–542, 2017*
- Epilepsy
  - At least two unprovoked (or reflex) seizures occurring >24 h apart
  - One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
  - Diagnosis of an epilepsy syndrome
    - complex of signs and symptoms that define a unique epileptic condition

# International League Against Epilepsy (ILAE) 2017 Seizure Classification

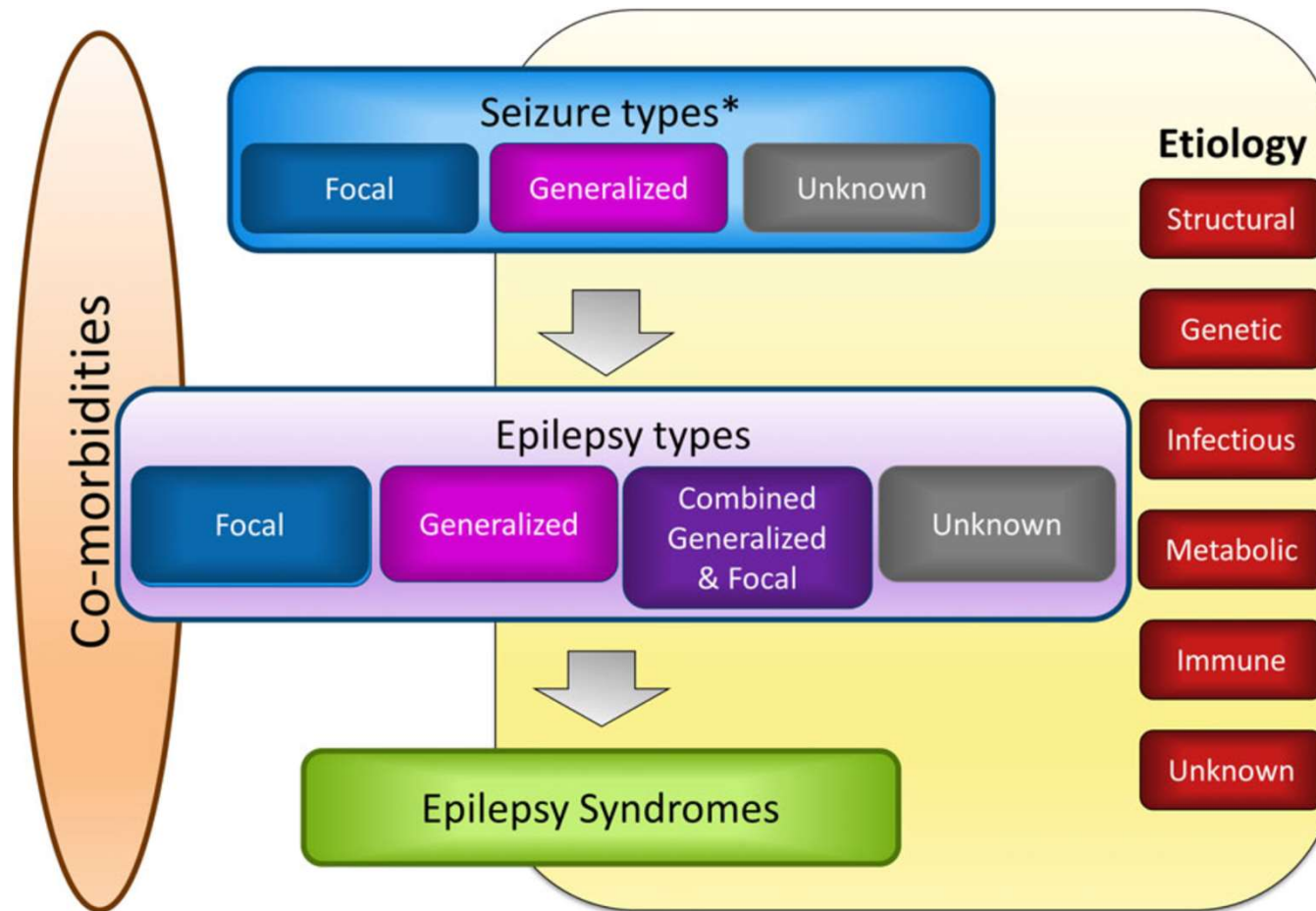
## Key Points

- The ILAE provided a revised basic and expanded seizure type classification, with initial division into:
  - Focal onset
  - Generalized onset
  - Unknown onset
- Focal seizures are optionally subdivided into focal aware and focal impaired awareness seizures
  - Specific motor and non-motor classifiers may be added
- Generalized-onset seizures can be:
  - Motor
  - Non-motor
- Additional descriptors and free text are encouraged to characterize the seizures
- Mapping of old to new terms can facilitate adoption of the new terminology

*Fisher RS et al Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia, 58(4):531–542, 2017*

## Summary of rules for classifying seizures

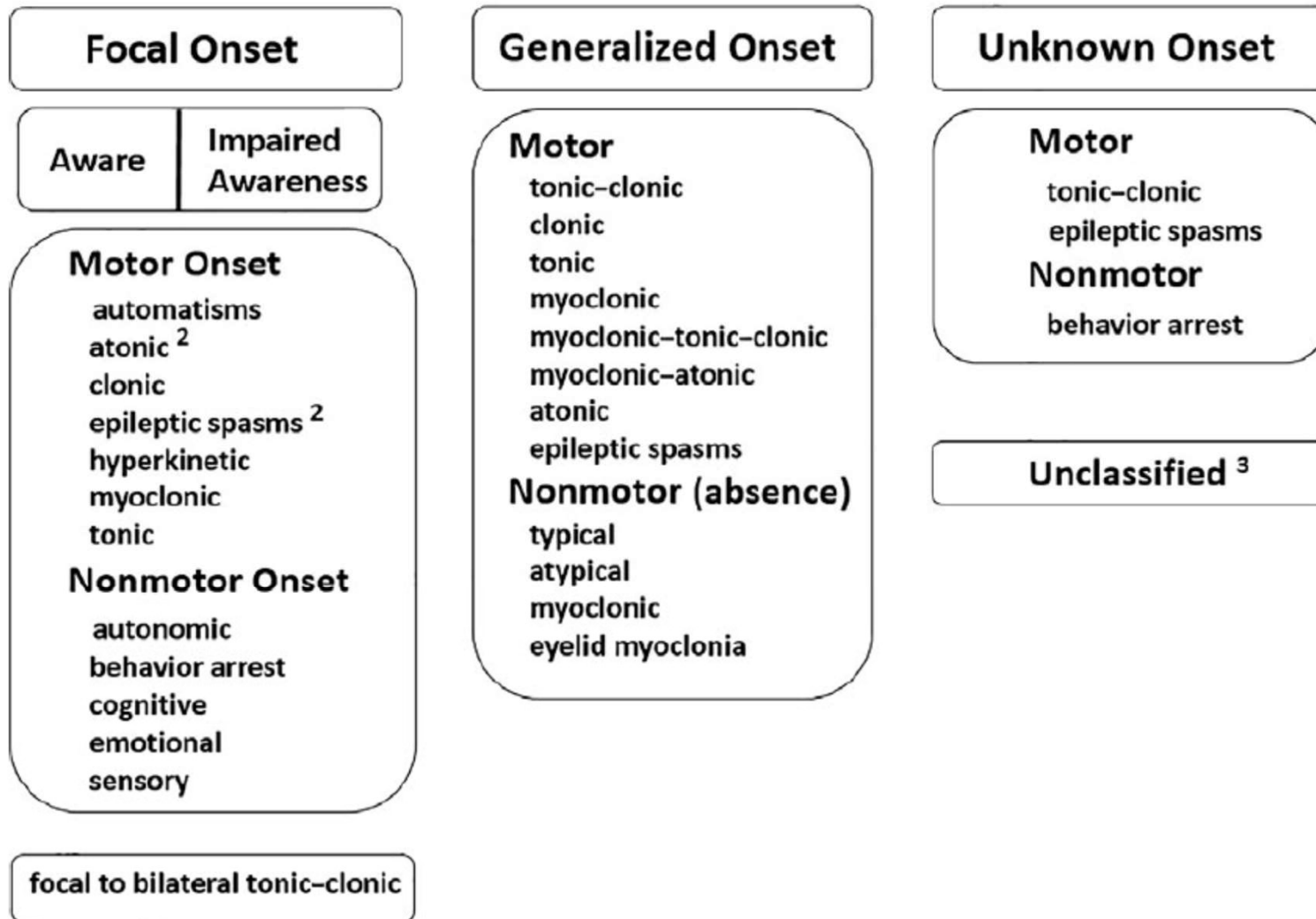
- 1 Onset: Decide whether seizure onset is focal or generalized, using an 80% confidence level. Otherwise, onset is unknown.
- 2 Awareness: For focal seizures, decide whether to classify by degree of awareness or to omit awareness as a classifier. *Focal aware seizures* correspond to the old *simple partial seizures* and *focal impaired awareness seizures* to the old *complex partial seizures*.
- 3 Impaired awareness at any point: A focal seizure is a *focal impaired awareness seizure* if awareness is impaired at any point during the seizure.
- 4 Onset predominates: Classify a focal seizure by its first prominent sign or symptom. Do not count transient behavior arrest.
- 5 Behavior arrest: A *focal behavior arrest seizure* shows arrest of behavior as the prominent feature of the entire seizure.
- 6 Motor/nonmotor: A *focal aware or impaired awareness seizure* may be further subclassified by motor or nonmotor characteristics. Alternatively, a focal seizure can be characterized by motor or nonmotor characteristics, without specifying level of awareness. Example, a *focal tonic seizure*.
- 7 Optional terms: Terms such as motor or nonmotor may be omitted when the seizure type is otherwise unambiguous.
- 8 Additional descriptors: After classifying seizure type based on initial manifestations, it is encouraged to add descriptions of other signs and symptoms, suggested descriptors or free text. These do not alter the seizure type. Example: *focal emotional seizure* with tonic right arm activity and hyperventilation.
- 9 Bilateral versus generalized: Use the term “bilateral” for tonic-clonic seizures that propagate to both hemispheres and “generalized” for seizures that apparently originate simultaneously in both hemispheres.
- 10 Atypical absence: Absence is atypical if it has slow onset or offset, marked changes in tone, or EEG spike-waves at <3 per second.
- 11 Clonic versus myoclonic: Clonic refers to sustained rhythmic jerking and myoclonic to regular unsustained jerking.
- 12 Eyelid myoclonia: *Absence with eyelid myoclonia* refers to forced upward jerking of the eyelids during an absence seizure.



*Scheffer et al Epilepsia 2017*

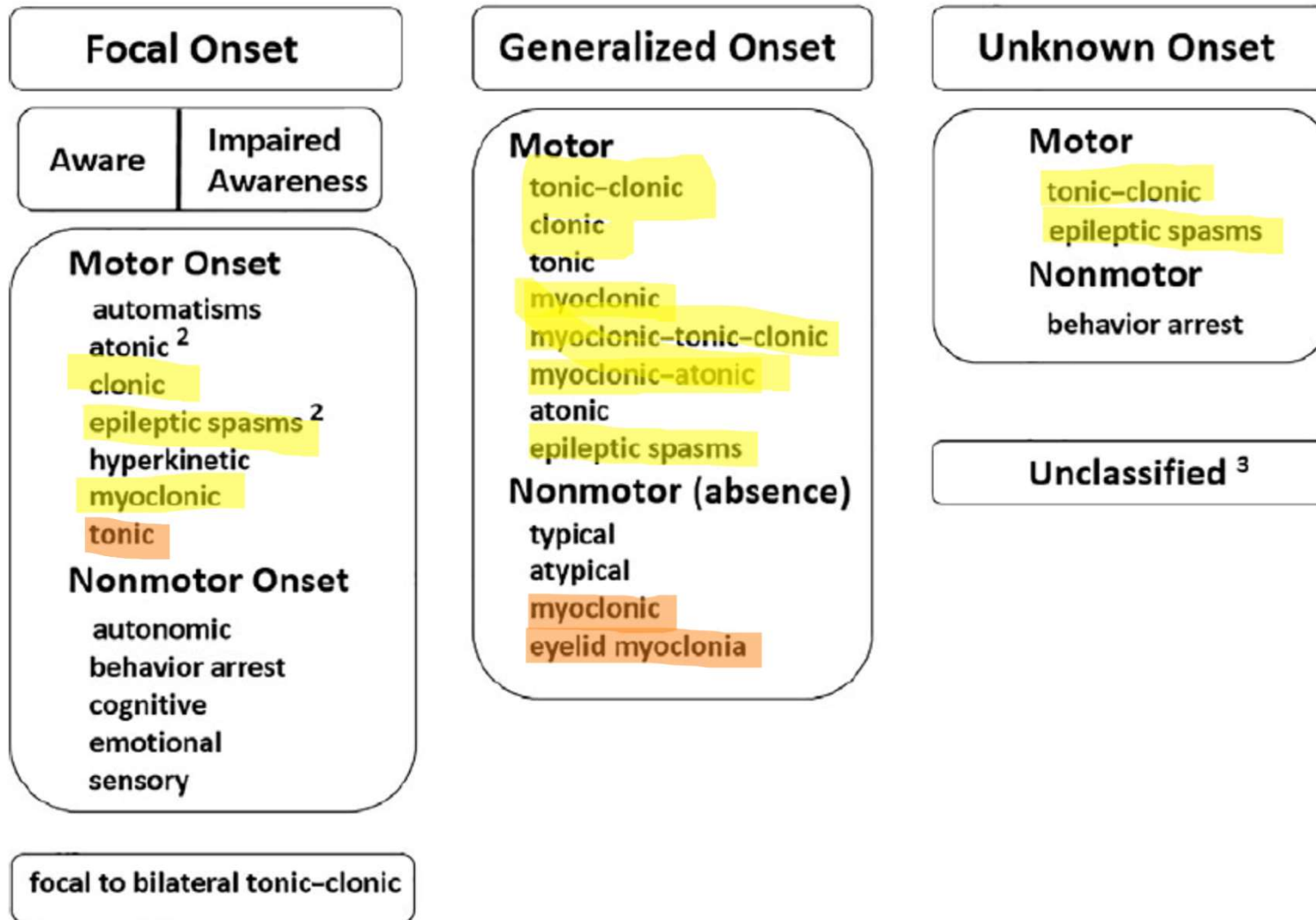


## ILAE 2017 Classification of Seizure Types Expanded Version <sup>1</sup>



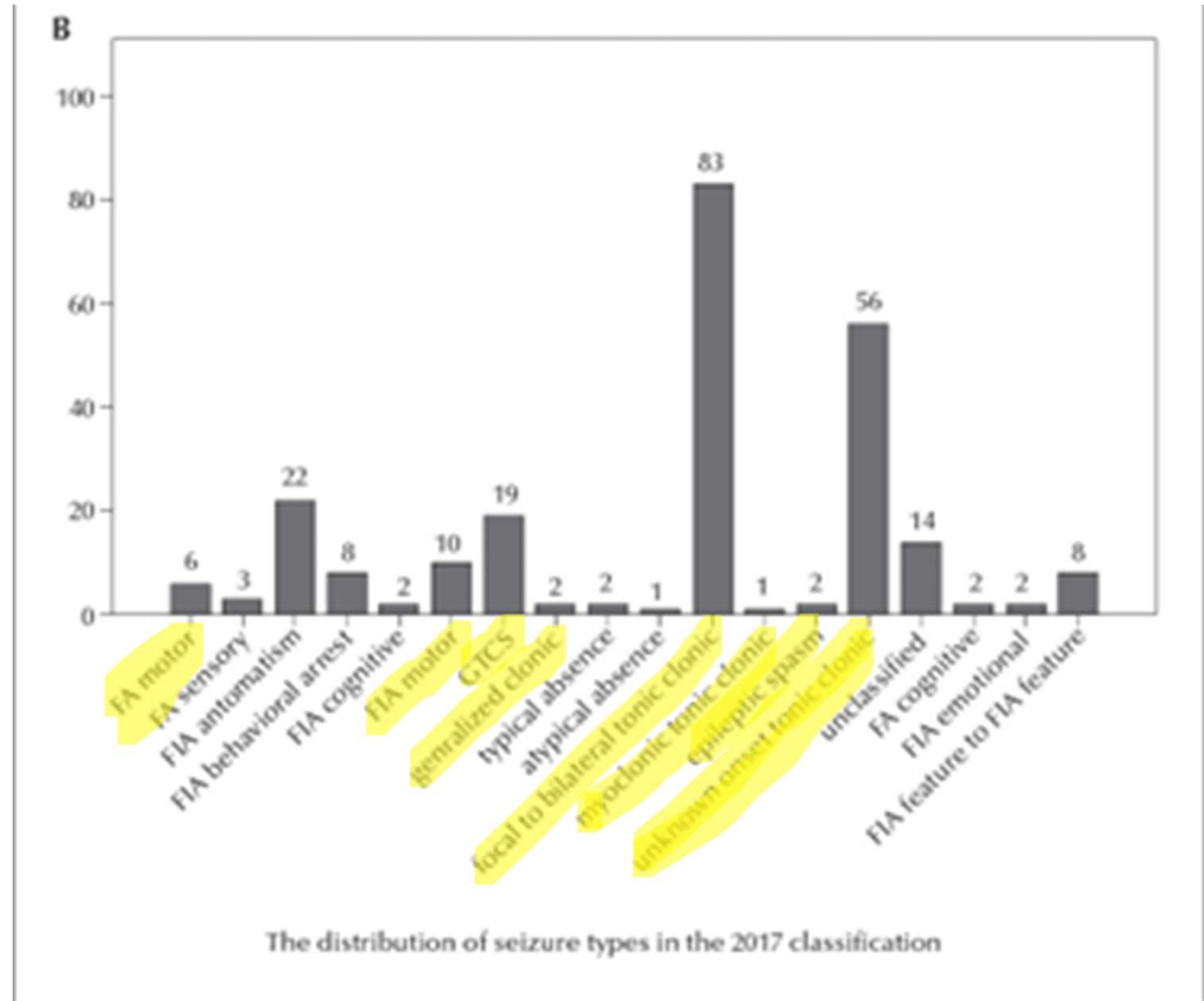


# ILAE 2017 Classification of Seizure Types Expanded Version



# Proportion with convulsive seizures

- 200 patients diagnose with epilepsy at a Chinese outpatients
- 50 had non-convulsive seizures
- *Gao et al Epileptic Disorders 2018*



# Proportion with convulsive seizures

- Population based study in Norwegian children
- 606 had a validated diagnosis of epilepsy
- Some children had more than one seizure type
- *Aaberg et al Epilepsia 2019*

Seizure type	Population proportion per 100,000, N = 112,744	All CWE, N = 606 <sup>d</sup>	
		n	%
ILAE 2017 seizure classification			
Focal onset seizures	369	416	69%
Focal onset aware	60	68	11%
Focal onset impaired awareness	330	372	61%
Focal to bilateral tonic-clonic	167	188	31%
Motor onset	266	300	50%
Nonmotor onset	157	177	29%
Generalized onset seizures	229	258	43%
Motor	176	198	33%
Tonic-clonic	99	112	19%
Clonic	0	—	—
Tonic	72	81	13%
Myoclonic	75	84	14%
Myoclonic-tonic-clonic	0	—	—
Myoclonic-atonic	4	5	1%
Atonic	35	39	6%
Epileptic spasms <sup>d</sup>	0	—	—
Nonmotor (absences)	101	114	19%
Typical absences	55	62	10%
Atypical absences	17	19	3%
Other absences (myoclonic, eyelid myoclonia, other)	32	36	6%
Unknown onset	127	143	24%
Motor	76	86	14%
Tonic-clonic not classifiable <sup>e</sup>	18	20	3%
Epileptic spasms <sup>d</sup>	53	60	10%
Nonmotor (behavioral arrest)	21	24	4%
Unclassified	31	35	6%

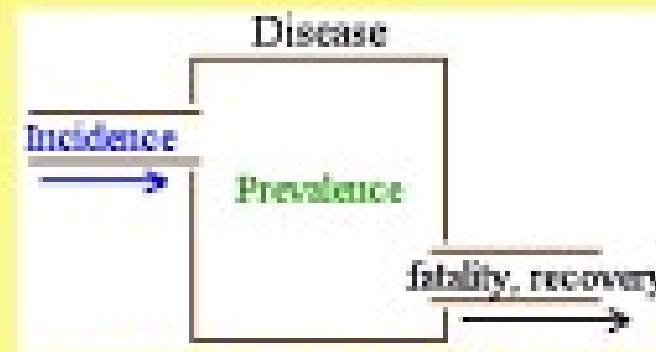
# Relationship between Epidemiological measures

- The incidence suggests that the prevalence should be much higher:

Prevalence = (Incidence Rate) x (Duration of Disease)

Duration = Spontaneous remission + premature mortality

## Prevalence vs. Incidence



- **Prevalence** can be viewed as describing a pool of disease in a population.
- **Incidence** describes the input flow of new cases into the pool.
- **Fatality and recovery** reflects the output flow from the pool.

# Prevalence

- A proportion: number of cases / total population
- Usually measured during cross-sectional survey
  - Sensitivity of the tools
  - Cases maybe hidden
- Difficulties in measuring the denominator

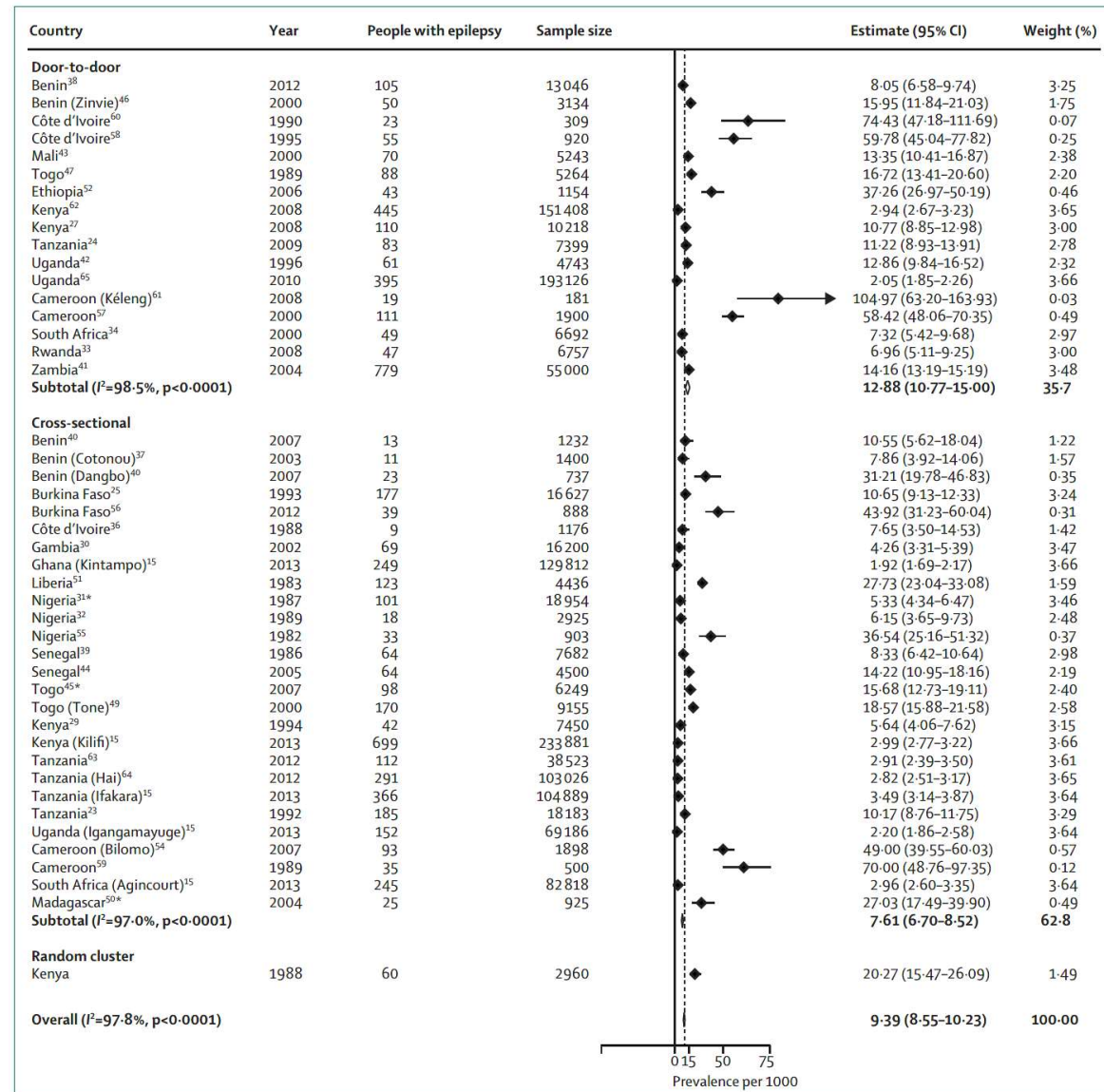


Figure 3: Meta-analysis of epilepsy prevalence in sub-Saharan Africa according to the type of study

\*Studies in which the estimates are based only on active epilepsy.

# Incidence

- Number of new cases per unit time – rate
- Diagnosed cases vs onset of seizures
- Difficult logistically and Expensive
  - Large cohort to be followed up over long time
- Most robust – follow a cohort with active surveillance of newly diagnosed cases
- Recall method
  - Using cross-sectional survey and determining number of cases in which the onset of seizures has occurred within 1 year or 5 years (less reliable) of the assessment
  - In Kilifi using recall of 1 year underestimated the incidence by 42.8%

	Year	N	Incidence (95% CI)*	Sex ratio (M/F)	Proportion aged <20 years	Type of study
Ethiopia <sup>21</sup>	1997	61 686	64.0 (44–84)	1.2	79.0%	Prospective
Benin (Djidja) <sup>22</sup>	2013	11 668	69.4 (30–137)	0.9	NA	Prospective
Tanzania <sup>23</sup>	1992	18 183	73.3 (34–113)	0.9	60.8%	Retrospective
Tanzania <sup>24</sup>	2009	7 399	81.0 (65–101)	1.0	59.1%	Prospective
Burkina Faso <sup>25</sup>	1993	16 627	83.0 (40–126)	1.7	76.2%	Retrospective
Uganda <sup>26</sup>	1998	4 389	156.0 (145–166)	1.2	97.5%	Prospective
Kenya <sup>27</sup>	2008	10 218	187.0 (133–256)	1.0	NA	Prospective
Kenya <sup>28</sup>	2013	623 004	77.0 (68–87)	0.9	54.5%	Retrospective

NA=not available. \*Per 100 000 person-years of follow-up.

**Table 1: Studies of the incidence of epilepsy in sub-Saharan Africa**

# Mortality

- Need to follow up a cohort of cases over a specified period of time
- Determine the cause of death
  - Autopsies
  - Verbal Autopsies
- Measured as
  - Case fatality
    - Proportion of deaths in a cohort of PWE
  - Standardised Mortality Ratio (SMR)
    - Compares rates of death in PWE to a reference population
  - Proportionate mortality
    - Number of deaths due to epilepsy in a population



# Remission

- Spontaneous remission
  - Requires follow up of a cohort
  - Difficulties with definition – period of seizure free varies: 1, 2 or 5 years
  - Can be calculated if the Incidence, Prevalence and Mortality is known

# Spontaneous Remission Rate

**Table 2. Prevalence, incidence, mean duration of disease, remission, and standardized mortality ratio estimated in DisMod II for epilepsy in Kilifi, 2008**

Age (years)	Prevalence per 1,000	Incidence per 100,000/year	Standardized mortality ratio	Instantaneous remission rate (%)	Proportion remitting per year
<b>Male</b>					
0-5	2.31 (0.82-3.81)	85.19 (29.05-93.32)	3.23 (3.08-3.25)	35.39 (3.02-68.82)	29.81 (2.97-49.75)
6-12	2.90 (1.03-4.84)	53.07 (7.42-56.75)	16.95 (16.40-17.94)	11.19 (0.00-30.50)	10.59 (0.00-26.29)
13-18	3.84 (1.24-6.62)	39.64 (6.26-42.72)	15.07 (13.39-16.05)	5.80 (0.00-30.50)	5.64 (0.00-26.29)
19-28	3.97 (1.11-5.92)	28.53 (5.93-30.39)	8.87 (8.84-9.34)	6.59 (0.00-13.54)	6.38 (0.00-12.66)
29-49	3.12 (0.99-4.97)	24.07 (6.30-25.64)	5.87 (5.43-6.17)	5.68 (0.00-11.59)	5.52 (0.00-10.94)
50+	3.13 (1.25-5.16)	43.52 (6.05-46.73)	8.72 (8.21-9.27)	8.59 (0.00-17.62)	8.23 (0.00-16.15)
All ages	3.16 (1.05-5.14)	48.00 (10.92-51.80)	10.80 (9.30-11.90)	11.60 (0.46-25.13)	10.95 (0.46-22.22)
<b>Female</b>					
0-5	1.86 (0.63-3.10)	69.44 (14.50-74.37)	1.70 (1.60-1.70)	35.93 (5.59-66.84)	30.18 (5.44-48.75)
6-12	2.42 (0.97-3.92)	48.20 (7.60-50.88)	6.88 (6.67-7.23)	12.74 (0.66-28.61)	11.96 (0.66-24.88)
13-18	3.71 (1.29-6.14)	41.36 (6.77-44.35)	9.79 (9.37-10.26)	5.36 (0.00-10.96)	5.22 (0.00-10.38)
19-28	3.58 (1.20-6.00)	33.83 (5.56-36.69)	7.75 (6.48-7.93)	11.71 (0.00-23.84)	11.05 (0.00-21.21)
29-49	2.06 (0.66-4.10)	14.95 (4.74-15.96)	2.97 (2.79-3.04)	8.13 (0.00-15.94)	7.81 (0.00-14.73)
50+	2.12 (0.89-3.42)	27.30 (5.46-29.31)	9.91 (9.53-10.47)	9.59 (0.01-19.51)	9.14 (0.01-17.72)
All ages	2.59 (0.92-4.41)	39.16 (7.47-41.89)	8.13 (8.06-8.53)	12.82 (0.79-25.47)	12.03 (0.79-22.49)

To obtain the proportion remitting per year the following formula was used  $1 - e^{(-\text{remission rate})}$ .

# Population Attributable Fraction (PAF)

- Population attributable risk is the number of new cases in a defined period that are due to (attributable to) a particular causative factor
- Population attributable fraction (PAF) is the reduction in the incidence of disease that would be expected in a population if a specific factor presumed to be causal is removed from the population

- $$PAF = \frac{p(RR-1)}{p(RR-1)+1}$$

Where p = prevalence of risk factor

RR = Relative Risk

- Used Odds ratio as an estimate of the RR
- Usually expressed as a fraction 0-1
- Used Greenland and Dreschler's maximum likelihood estimator (*Biometrics 1993 49, 865*)

# Population Attributable Fraction

	All sites	Agincourt S Africa	Ifakara Tanzania	Iganga Uganda	Kilifi Kenya	Kintampo Ghana
<b>Non-parasitic adults:</b>						
seizures in family, maternal seizures, problems after delivery, place delivery, head injury, cassava	0.38 (0.13,0.55)	0.34 (0.09,0.52)	0.32 (0.11,0.48)	0.35 (0.09,0.54)	0.35 (0.08,0.54)	0.46 (0.20,0.63)
<b>Non-parasitic children</b>						
seizures in family, maternal seizures, abnormal pregnancy, problems after delivery, place delivery, perinatal difficulties head injury	0.40 (0.31,0.48)	0.25 (0.16,0.33)	0.30 (0.22,0.38)	0.27 (0.20,0.34)	0.46 (0.33,0.56)	0.62 (0.50,0.71)
<b>T.canis+T.gondii</b> (children+adults)	0.15 (0.07,0.23)	0.06 (0.02,0.09)	0.39 (0.15,0.53)	0.12 (0.05,0.19)	0.17 (0.08,0.25)	0.21 (0.08,0.32)
<b>T.canis+T.gondii+Oncho</b> (children+adults)	0.28 (0.14,0.39)		0.44 (0.25,0.62)	0.09 (0.02,0.19)		0.36 (0.20,0.50)

(95% Confidence Intervals)

*Ngugi et al Lancet Neurology 2013*

# Population Attributable Fraction

	All sites	Agincourt S Africa	Ifakara Tanzania	Iganga Uganda	Kilifi Kenya	Kintampo Ghana
<b>Non-parasitic adults:</b> seizures in family, maternal seizures, problems after delivery, place delivery, head injury, cassava	0.38 (0.13,0.55)	0.34 (0.09,0.52)	0.32 (0.11,0.48)	0.35 (0.09,0.54)	0.35 (0.08,0.54)	0.46 (0.20,0.63)
<b>Non-parasitic children</b> seizures in family, maternal seizures, abnormal pregnancy, problems after delivery, place delivery, perinatal difficulties head injury	0.40 (0.31,0.48)	0.25 (0.16,0.33)	0.30 (0.22,0.38)	0.27 (0.20,0.34)	0.46 (0.33,0.56)	0.62 (0.50,0.71)
<b>T.canis+T.gondii</b> (children+adults)	0.15 (0.07,0.23)	0.06 (0.02,0.09)	0.39 (0.15,0.53)	0.12 (0.05,0.19)	0.17 (0.08,0.25)	0.21 (0.08,0.32)
<b>T.canis+T.gondii+Oncho</b> (children+adults)	0.28 (0.14,0.39)		0.44 (0.25,0.62)	0.09 (0.02,0.19)		0.36 (0.20,0.50)

# Population Attributable Fraction in Adults

	All sites	Agincourt S Africa	Ifakara Tanzania	Iganga Uganda	Kilifi Kenya	Kintampo Ghana
<b>Non-parasitic adults:</b> seizures in family, maternal seizures, problems after delivery, place delivery, head injury, cassava	0.38 (0.13,0.55)	0.34 (0.09,0.52)	0.32 (0.11,0.48)	0.35 (0.09,0.54)	0.35 (0.08,0.54)	0.46 (0.20,0.63)
<b>Infections and Parasites</b>	0.35 (0.24,0.44)	0.09 (0.04,0.14)	0.62 (0.44,0.74)	0.28 (0.12,0.40)	0.31 (0.16,0.44)	0.52 (0.44,0.65)
<b>T.canis+T.gondii+Oncho</b>	0.28 (0.14,0.39)		0.44 (0.25,0.62)	0.09 (0.02,0.19)		0.36 (0.20,0.50)

# Conclusions

- Epidemiological studies are difficult and the results must be interpreted with caution
- Most epidemiological studies conducted in Africa underestimate the burden of epilepsy
  - People with epilepsy - hidden or hide
  - Poor epidemiological infra-structure
  - do not account for non-convulsive seizures
- Incidence studies are very difficult to conduct