Epidemiology of Epilepsy

Charles Newton
Kilifi, Kenya
Dar-es-Salaam, Tanzania
University of Oxford, UK
University College London, UK

wellcome trust

Kenya Medical Research Institute/Wellcome Trust Supported Collaborative Programme

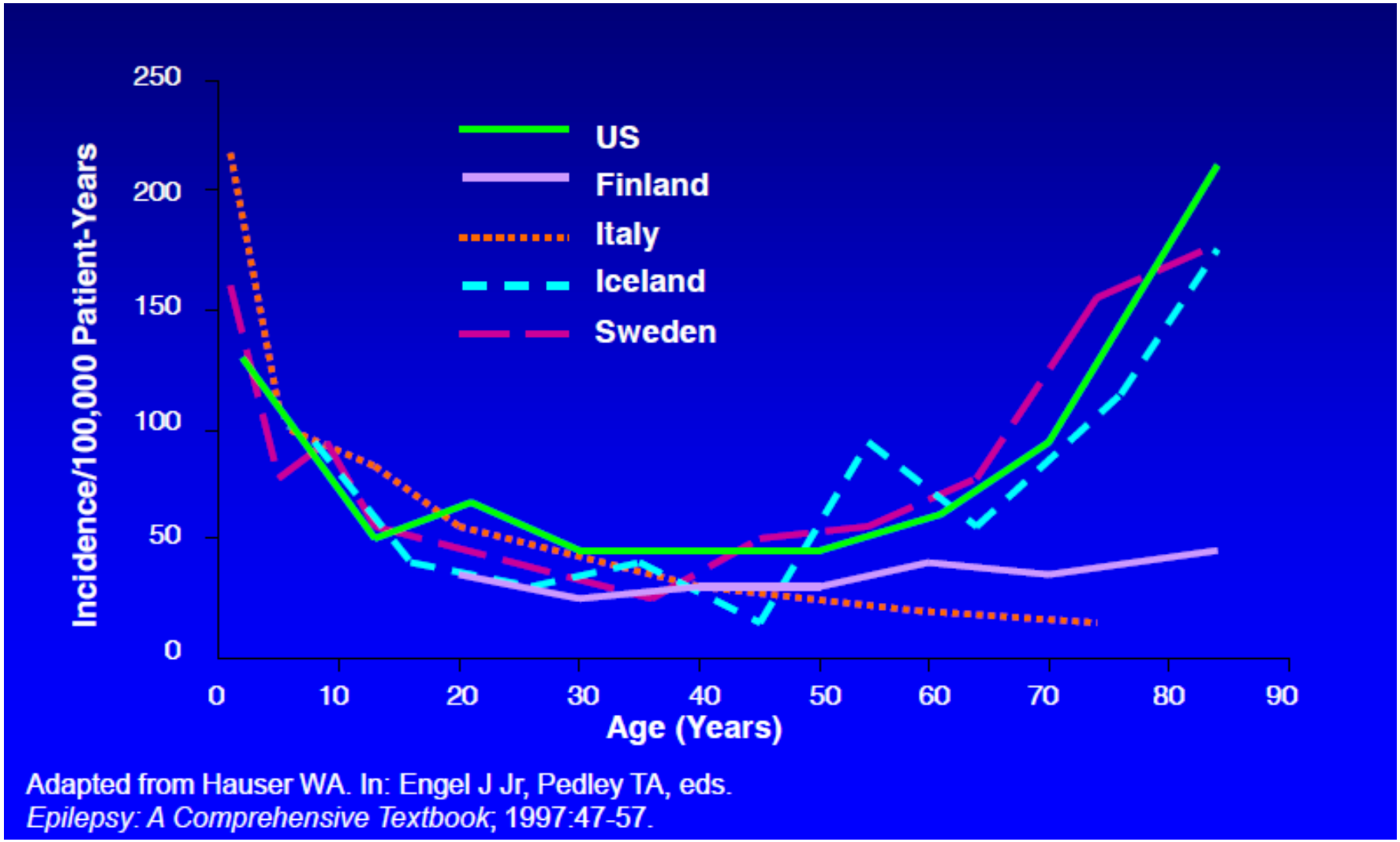
Global Burden of Epilepsy

- 0.5-1% of the Global Burden of Disease (GBD)
- estimated 7 million disability adjusted life years annually
- 22% of the burden estimated to be in 1 billion people in Africa (14% World Population)
- Risk of having at least 1 seizure in lifetime is 10%, and 1/3 will develop epilepsy

Epidemiological Definitions

- Incidence
  - Number of new cases per period of time
  - Rate
- Prevalence
  - Number of cases per population
  - Ratio

Incidence according to Age



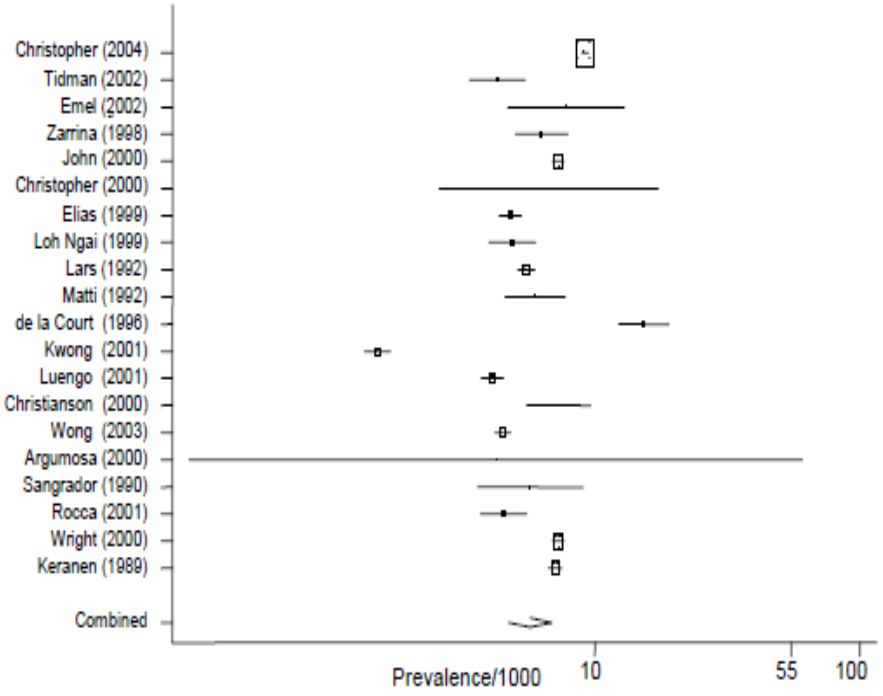
Adapted from Hauser WA. In: Engel J Jr, Pedley TA, eds. *Epilepsy: A Comprehensive Textbook*; 1997:47-57.

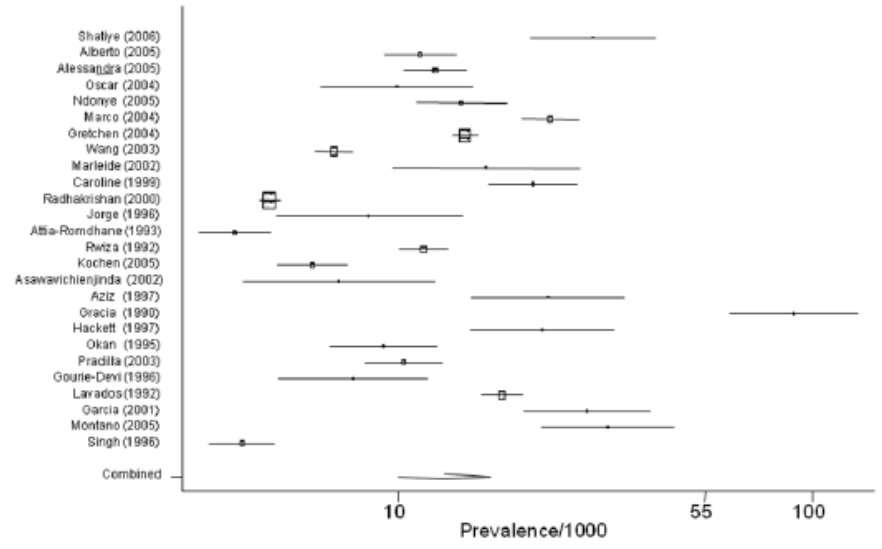
Meta-analysis of prevalence studies

- Global Burden 69M
- Resource Rich countries median 5.8/1000
- Resource Poor countries
  - rural areas 15.4 (4.8–49.6)
  - urban 10.3 (2.8–37.7)
- Heterogeneity accounted for by
  - country development (31.7%)
  - study size (26.4%)

Ngugi et al Epilepsia 2010; 51(5):883–890

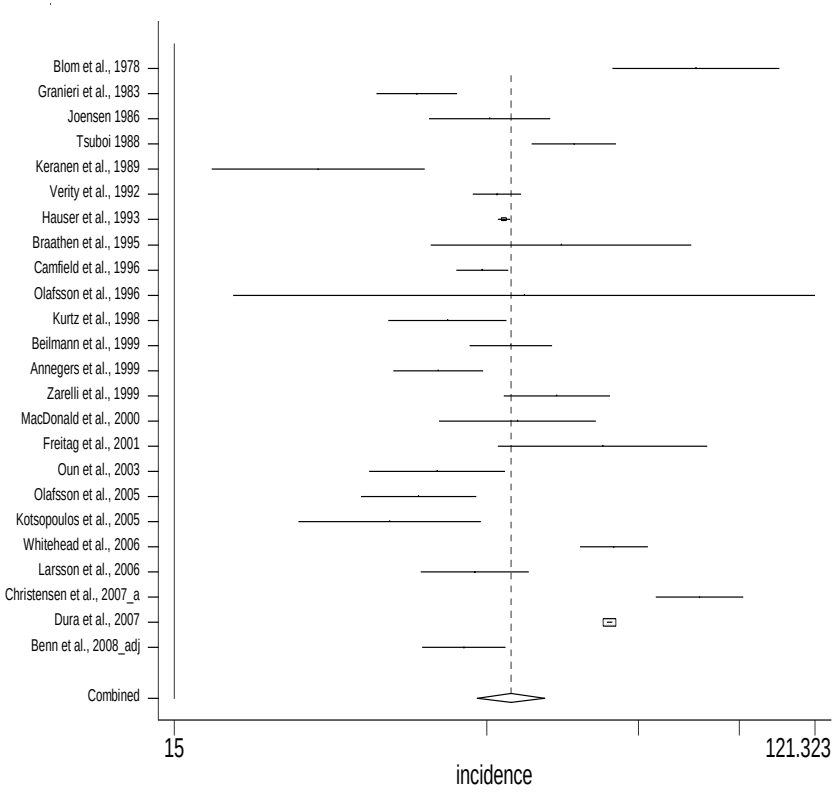
Figure 3: Forest Plot for the LTE prevalence data from developed countries.



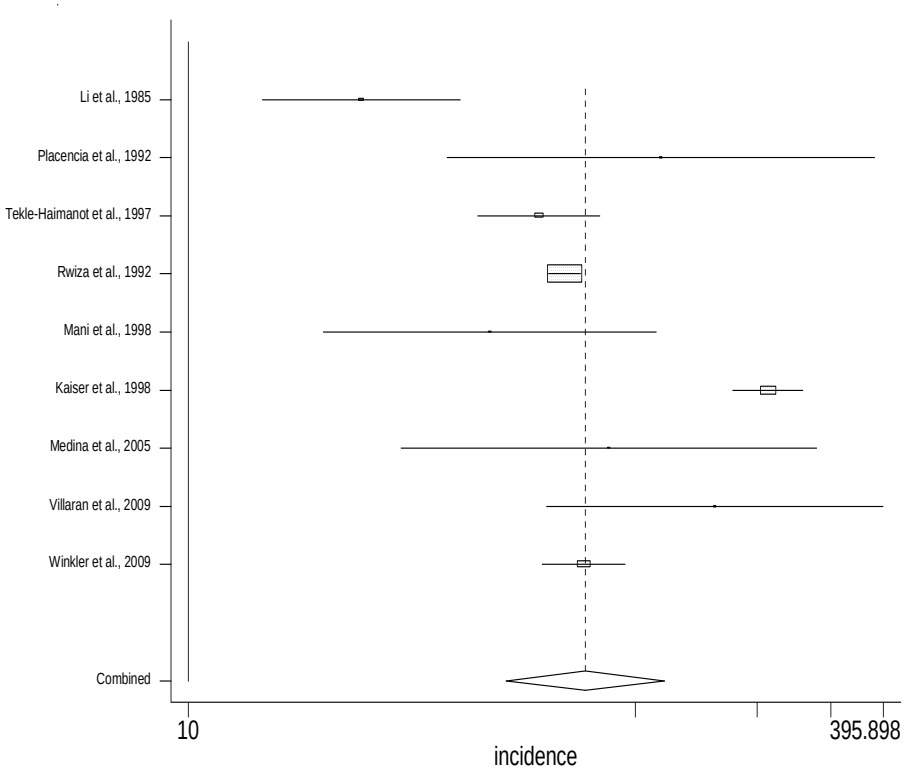


Heterogeneity in incidence studies

High Income countries



Low & Middle Income Countries



Ngugi AK et al., 2011

Determination of Active Convulsive Epilepsy (ACE)

- Non-convulsive seizures unreliably detected in Africa

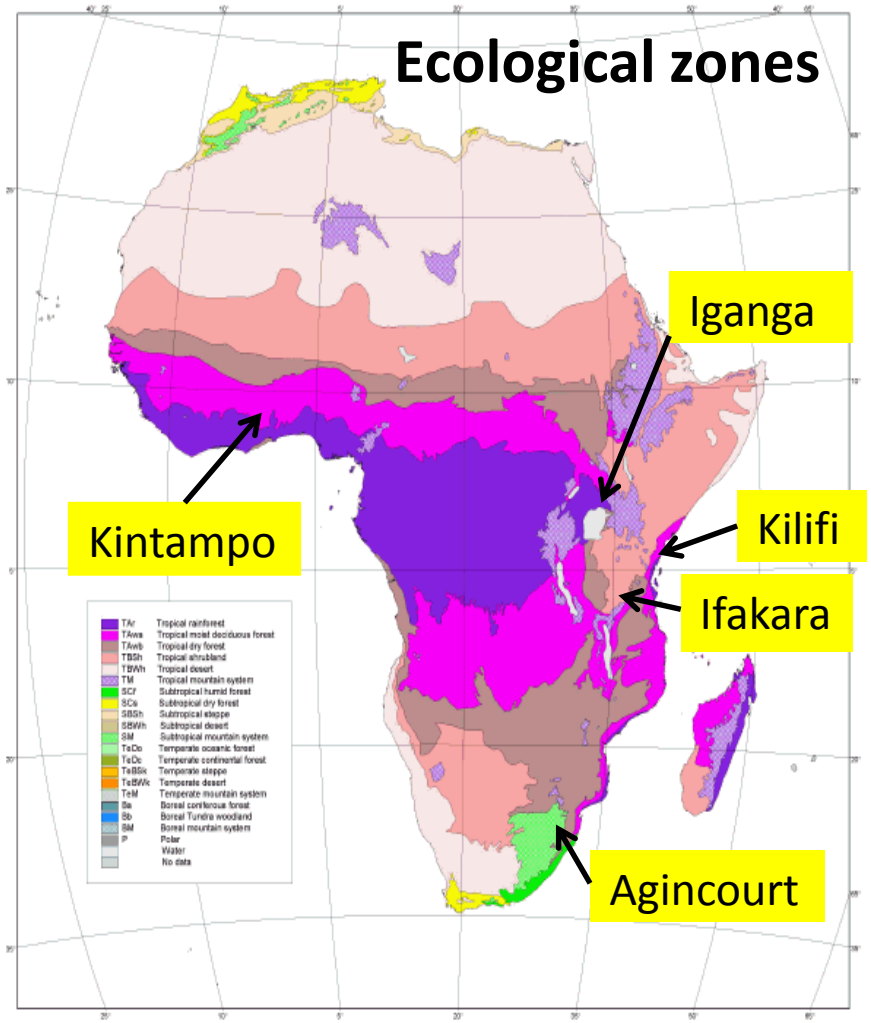
  Newton et al S Afr Med J 1984; 66: 21-23

- 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
- Convulsive epilepsy associated with
  - Most stigma
  - Morbidity e.g. burns
  - Mortality
- Epilepsy
  - 2 or more unprovoked seizures in a lifetime

Studies of Epidemiology of Epilepsy in Demographic Sites (SEEDS)

- Choose to conduct the studies in Health and Demographic Surveillance Systems (INDEPTH):
  - accurate denominators
  - able to identify subjects for follow-up
  - able to measure mortality
- 5 Sites chosen for
  - endemicity of parasitic risk factors
    - Neurocysticersosis (*Taenia sp*)
    - Onchocerciasis
    - *Toxocara sp*
    - *Toxoplasmosis gondii*
    - Malaria (*P. falciparum*)
  - neurological support
  - cost and logistical



Prevalence of ACE in Africa

Site	Population	Cases fulfilled definition of residency	Crude prevalence (95% CI) /1000	Adjusted prevalence (95% CI) /1000	Controls
Agincourt S Africa	83,121	245	3.0 (2.6-3.3)	7.0 (6.2-7.4)	261
Ifakara Tanzania	104,889	366	3.9 (3.5-4.3)	14.8 (13.8-15.4)	625
Iganga Uganda	69,186	152	2.4 (2.0-2.8)	10.3 (9.5-11.1)	239
Kilifi Kenya	233,881	699	3.0 (2.8-3.2)	7.8 (7.5-8.2)	527
Kintampo Ghana	129,812	249	2.2 (1.9-2.5)	10.1 (9.5-10.7)	381
TOTAL	**620,889**	**1,711**			**2,033**

Ngugi AN, Bottomley CB et al Lancet Neurology 2013

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Age-specific Prevalence & Age of Onset

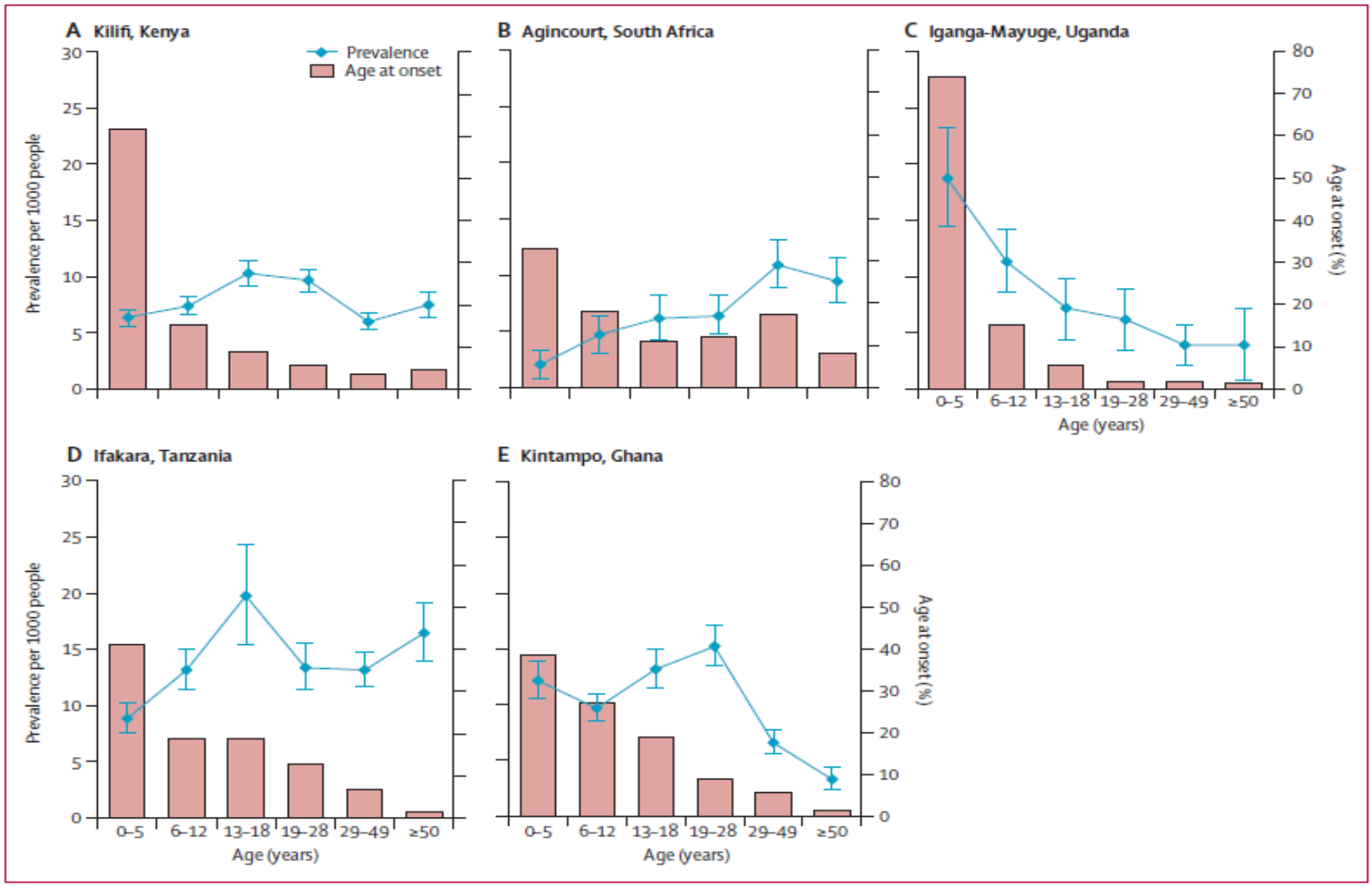

Figure: Age-specific prevalence and age at onset of active convulsive epilepsy in the five centres

Risk Factors for Epilepsy

- In newborns and infants:
  - Genetic factors (Family History)
  - Congenital (present at birth)
  - Prematurity
  - Perinatal disorders
  - Fever/infection
  - Metabolic
- In children, adolescents, and young adults:
  - Genetic factors
  - Congenital conditions
  - Perinatal disorders
  - Febrile Seizures
  - CNS Infection
  - Trauma to the head or brain injury

- Other possible causes of seizures may include:
  - Brain tumour
  - Neurological problems
  - Drug withdrawal
  - Medications
  - Use of illicit drugs
  - Alcohol or drugs

Risk Factors for ACE

Risk factor	% Cases	% Controls	OR* (95% CI)	P-value
Seizures in the family	20.4	11.4	2.04 (1.71,2.44)	<0.001
Maternal seizures	2.0	0.6	3.41 (1.78,6.56)	<0.001
Abnormal delivery	5.1	4.0	1.32 (0.97,1.79)	0.08
Abnormal pregnancy	14.4	6.5	2.30 (1.68,3.15)	<0.001
Home delivery	64.7	58.5	1.16 (1.00,1.36)	0.052
Problems after delivery	8.8	2.5	3.68 (2.65,5.12)	<0.001
Head injury before first seizure	8.8	6.0	1.37 (1.07,1.76)	0.013
Drinks alcohol	18.0	20.7	0.81 (0.64,1.03)	0.083
Eats cassava	82.5	75.4	1.46 (1.15,1.85)	0.002
Hypertension	1.7	1.1	1.65 (0.94,2.90)	0.08
Stroke	0.9	0.4	2.25 (0.96,5.29)	0.063
Dogs in household	40.1	47.6	0.82 (0.67,1.00)	0.053
Cats in household	44.8	46.6	1.06 (0.85,1.33)	0.604

*OR adjusted for age, sex, education (mother's education if under18 years) and country

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Parasitic Risk Factors

	Cases	Controls	Odds Ratio	P-value
Malaria (schizont)	83.6%	82.8%	1.13 (0.86,1.49)	0.37
Toxocara canis	26.5%	21.1%	1.32 (1.06,1.66)	0.014
Toxoplasmosis gondii	42.3%	35.4%	1.32 (1.10,1.58)	0.003
Taenia solium	3.2%	3.5%	0.71 (0.33,1.54)	0.388
Onchocerciasis	35.9%	22.6%	1.80 (1.42,2.27)	<0.001
HIV +ve	16.1%	14.0%	1.14 (0.90,1.43)	0.283

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Population Attributable Fraction (PAF)

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

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
Non-parasitic adults: 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)
Non-parasitic children 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)
T.canis+T.gondii (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)
T.canis+T.gondii+Oncho (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)

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Population Attributable Fraction in Children

	All sites	Agincourt S Africa	Ifakara Tanzania	Iganga Uganda	Kilifi Kenya	Kintampo Ghana
Non-parasitic children abnormal pregnancy, problems after delivery, place delivery, perinatal difficulties	0.33 (0.21,0.43)	0.22 (0.10,0.32)	0.25 (0.15,0.33)	0.18 (0.10,0.25)	0.39 (0.22,0.52)	0.51 (0.36,0.53)
Parasites and Infections	0.13 (0.01,0.24)	0.00 (-0.03,0.04)	0.27 (0.05,0.44)	0.09 (-0.02,0.18)	0.08 (-0.07,0.20)	0.22 (0.05,0.37)

Population Attributable Fraction in Adults

	All sites	Agincourt S Africa	Ifakara Tanzania	Iganga Uganda	Kilifi Kenya	Kintampo Ghana
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Infections and Parasites	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)
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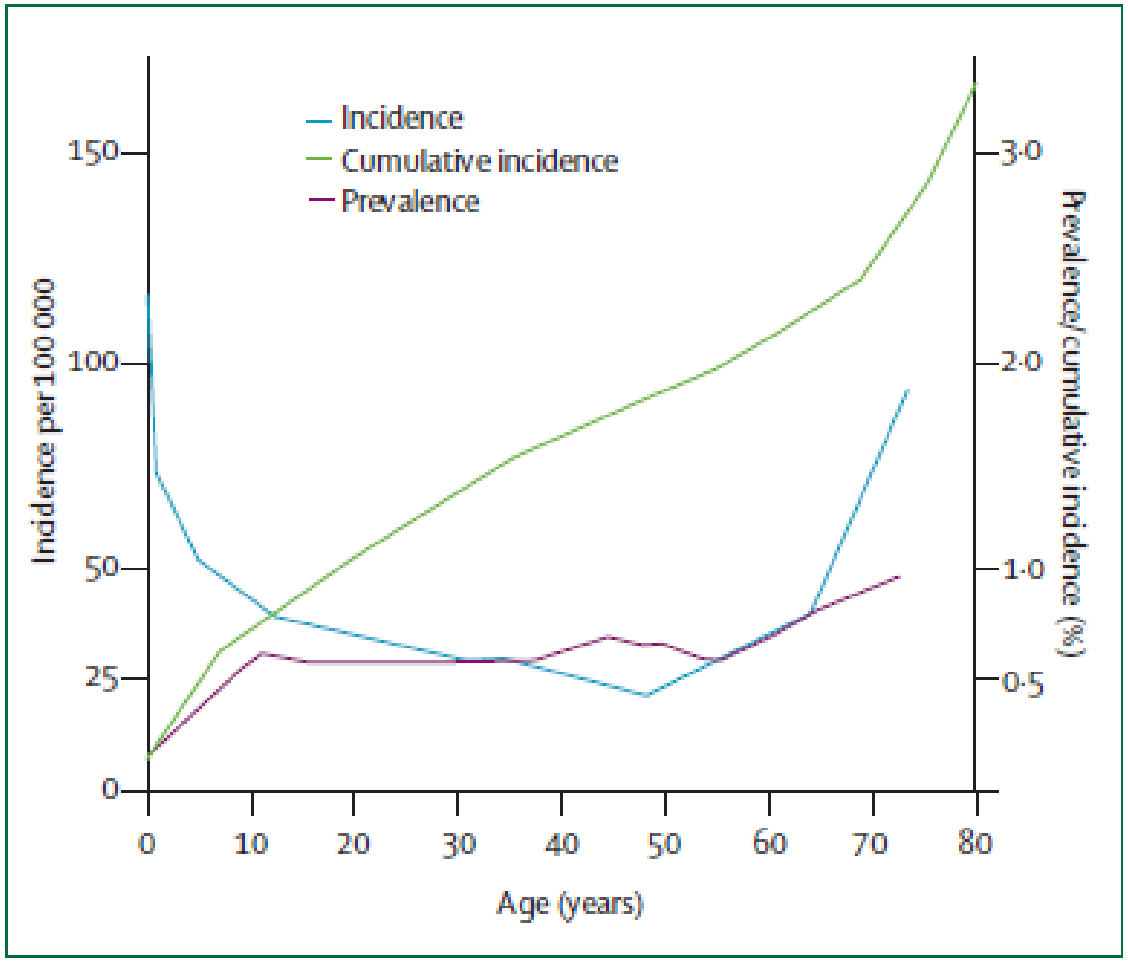
- Cumulative incidence increases to over 3%



Conundrum

- Given the high incidence rates observed, why is prevalence (at least lifetime) not much higher in developing countries?

$$Prevalence = Incidence\ x\ Duration\ of\ Condition$$

So …

- Given the high incidence rates observed, why is prevalence (at least lifetime) not much higher in developing countries?

$$\text{Prevalence} = \frac{75 \text{ x } 30}{100{,}000} = 22.5/1000$$

- Is it due to:
    1) Spontaneous remission?
    2) Differential survival?

Mortality in Epilepsy

- In the West:

  Standardised Mortality Ratios (SMR) ~ 1.6 – 4.1

  Highest in children & the elderly

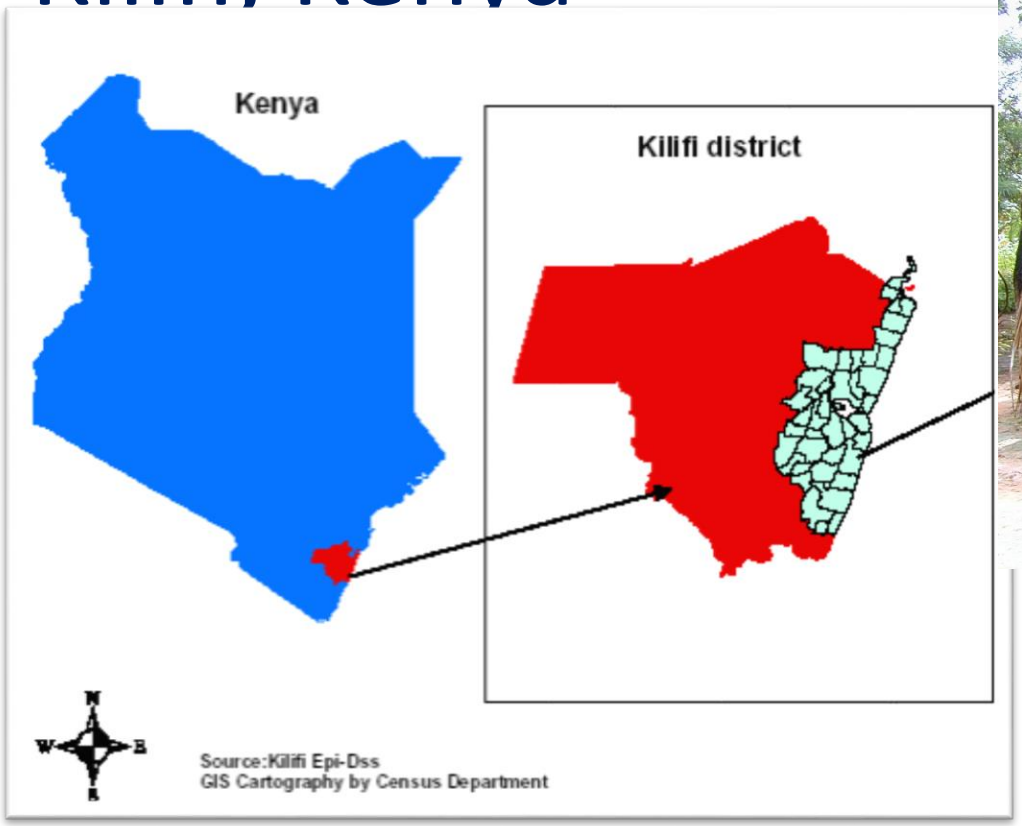
- Few studies in Africa

  SMR ~ 3-7

  Use diverse measurements

  Highest in adolescents & young adults

Kilifi, Kenya

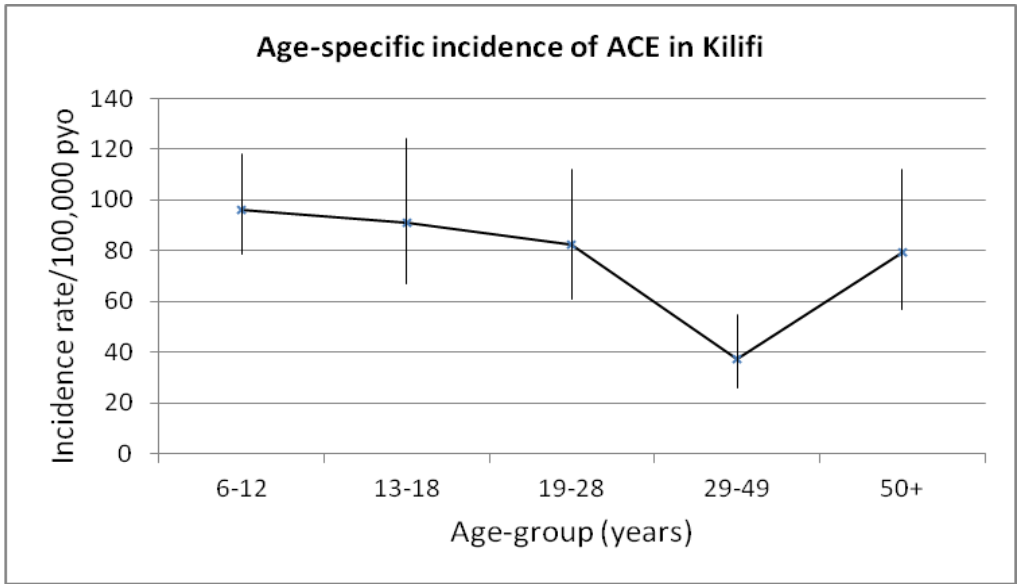


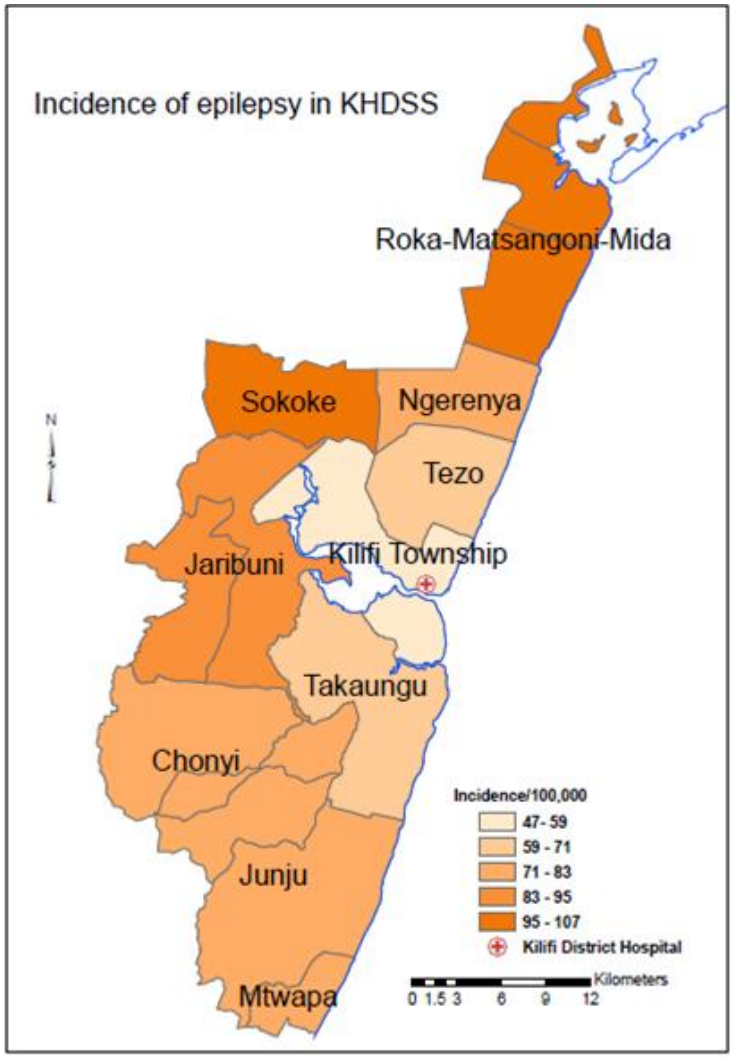
- 2nd poorest district in Kenya
- Average income 8 US dollars per month per capita
- 55% is considered poor
- 80% depend on subsistence farming
- Literacy levels are low (45%)

Permissions have been obtained to show these photographs

Incidence of ACE in Kilifi

- New cases between 2 surveys 2003-2008
- 194 people developed ACE:
  - crude incidence rate was 37.6/100,000 persons/year (95%CI: 32.7–43.3)
  - Adjusted incidence rate 77.0/100,000 persons/year (95%CI: 67.7–87.4)





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Mortality from in ACE in Kilifi

- Monitoring a cohort of ACE from 2003-2008
- 25 deaths in 437 people with ACE
- 70% causes are epilepsy related
  - Status epilepticus
  - drowning/burns

Age group	Standardized Mortality Ratio
(yrs)	(95% CI)
6-12	8.0 (2.6-24.8)
13-17	**25.7 (12.2-53.8)**
18-28	3.7 (1.4-10.0)
29-49	5.4 (2.7-10.9)
50+	0.9 (0.3-2.6)
Total	3.7 (2.5-5.5)

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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
Male					
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)
Female					
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 $1 - e^{(-\text{remission rate})}$.

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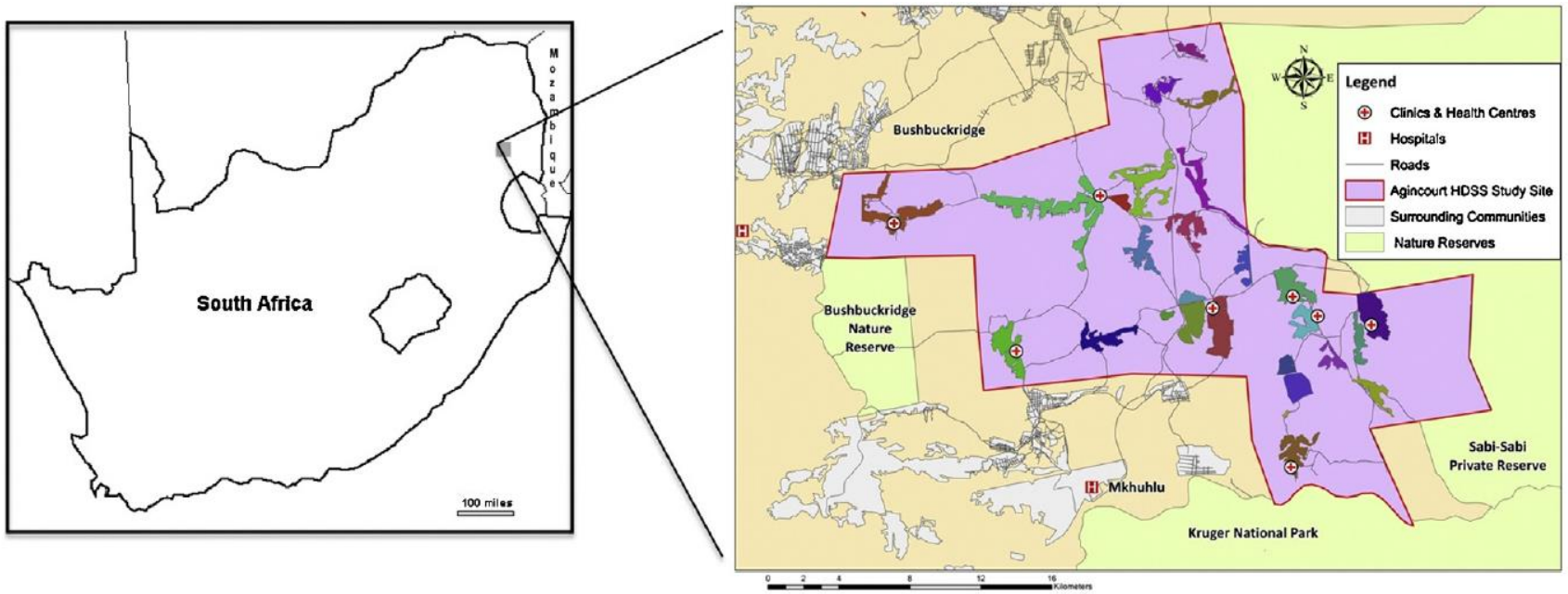
Studies in Mpumalanga, South Africa

- In 2008 population 83,121
- 32.8% originally from Mozambique



Parameters in Agincourt, South Africa

Age Band	Prevalence per 1000	Incidence Per 10,000/yr	Remission rate %/yr	Mortality Rate Per 1000/yr
0-5	2.18	11.9	2.3	23.5
6-12	4.78	21.4	4.5	20.5
13-18	6.38	7.4	2.5	15.2
19-28	6.23	17.2	5.3	13.6
29-49	10.95	24.0	1.5	16.3
50+	9.55	96.7	4.2	22.8
All	7.00	29.4	4.3	17.4

Conclusions

- Epilepsy is a major cause of neurological problems in Africa
- Most of epilepsy in Africa starts during childhood
- The prevalence is not higher because of the increased mortality

Human Immunodeficiency Virus

In 2013

- More than 29 million people now live with HIV/AIDS
  - 3 million < 15 years
  - 91% of children live in sub-Saharan Africa
- Estimated 1.8 million people were newly infected with HIV
  - 300,000 < 15 years
- 1.3 million people died from AIDS,
    - 200,000 < 15 years

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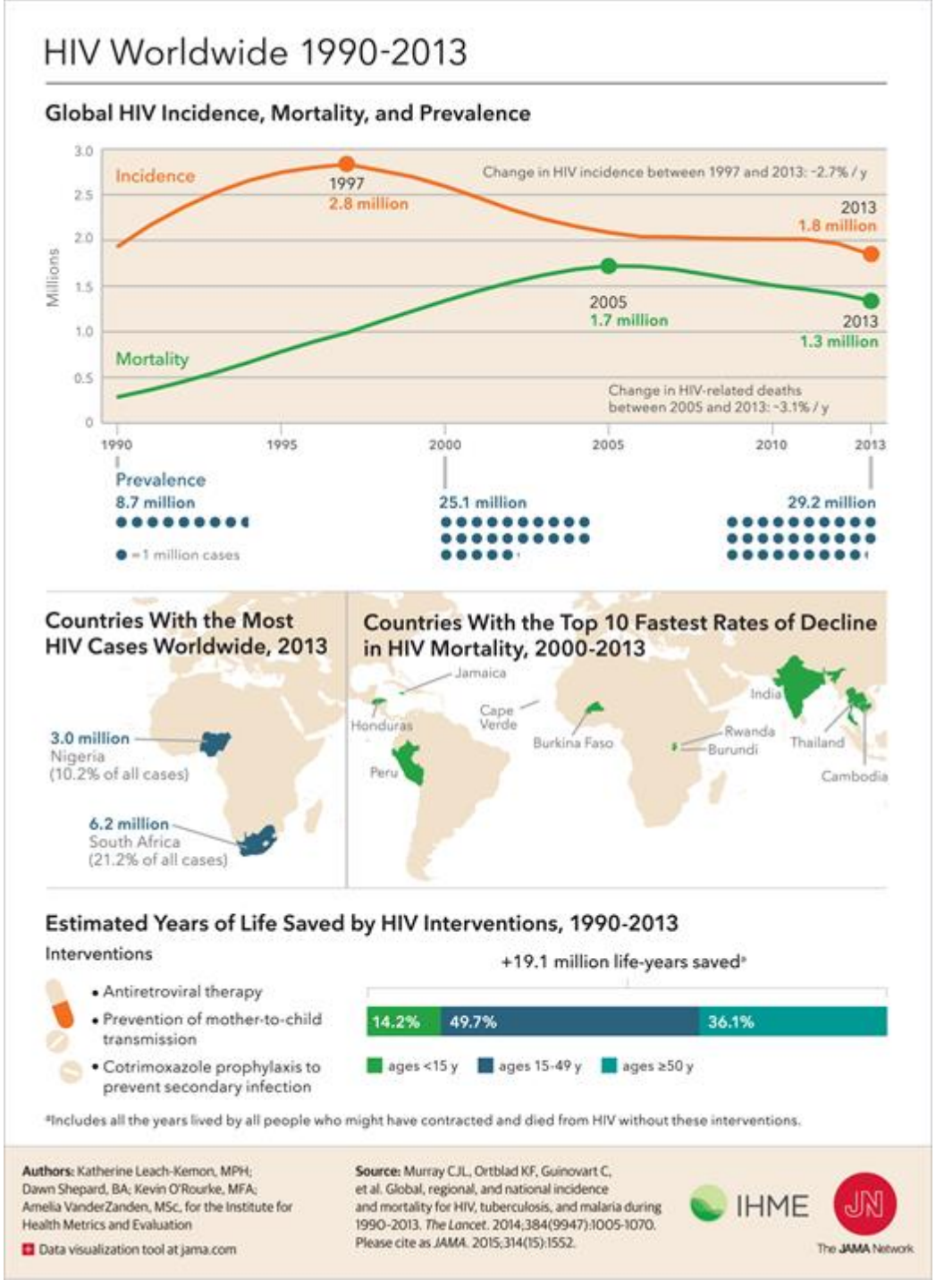
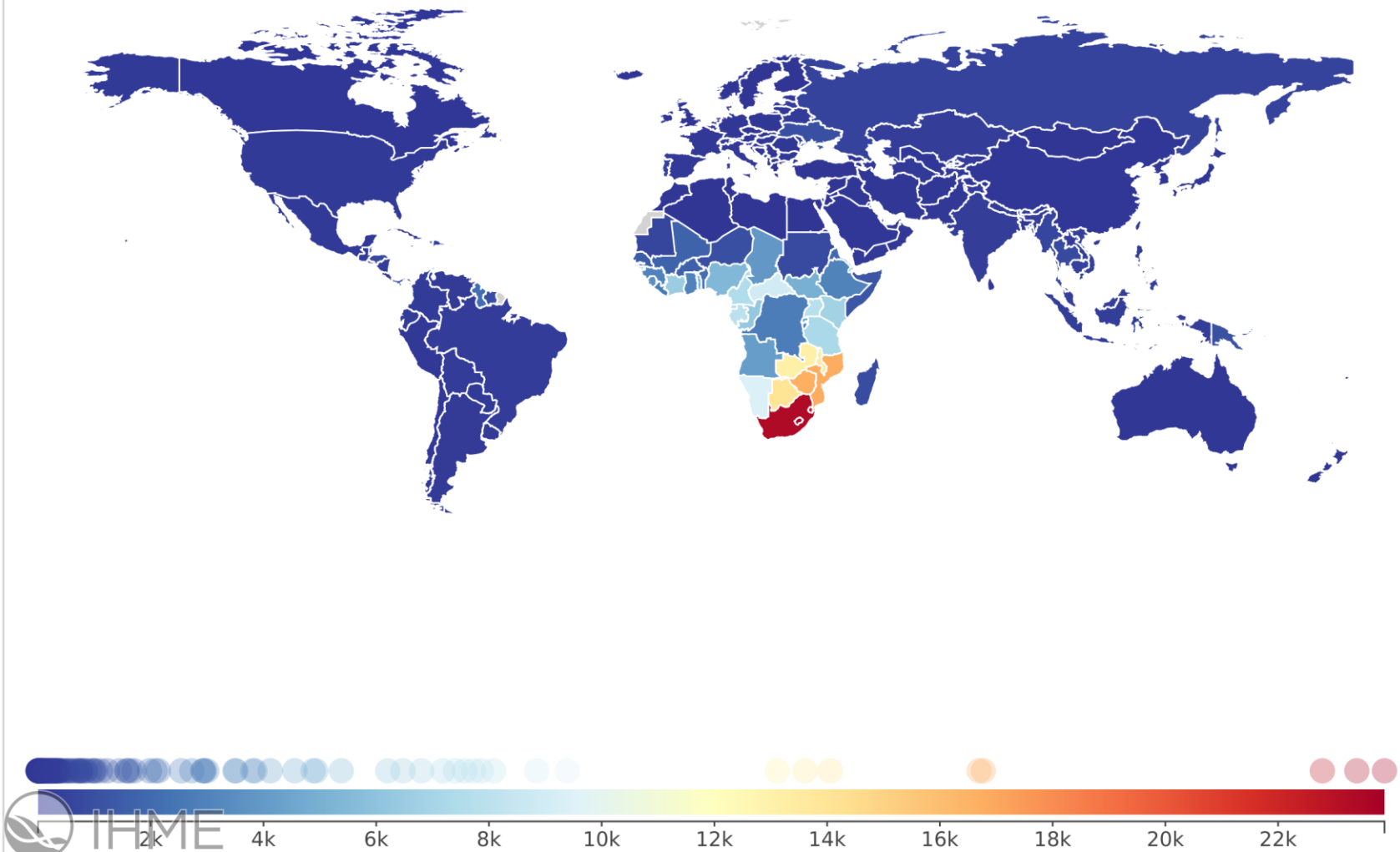
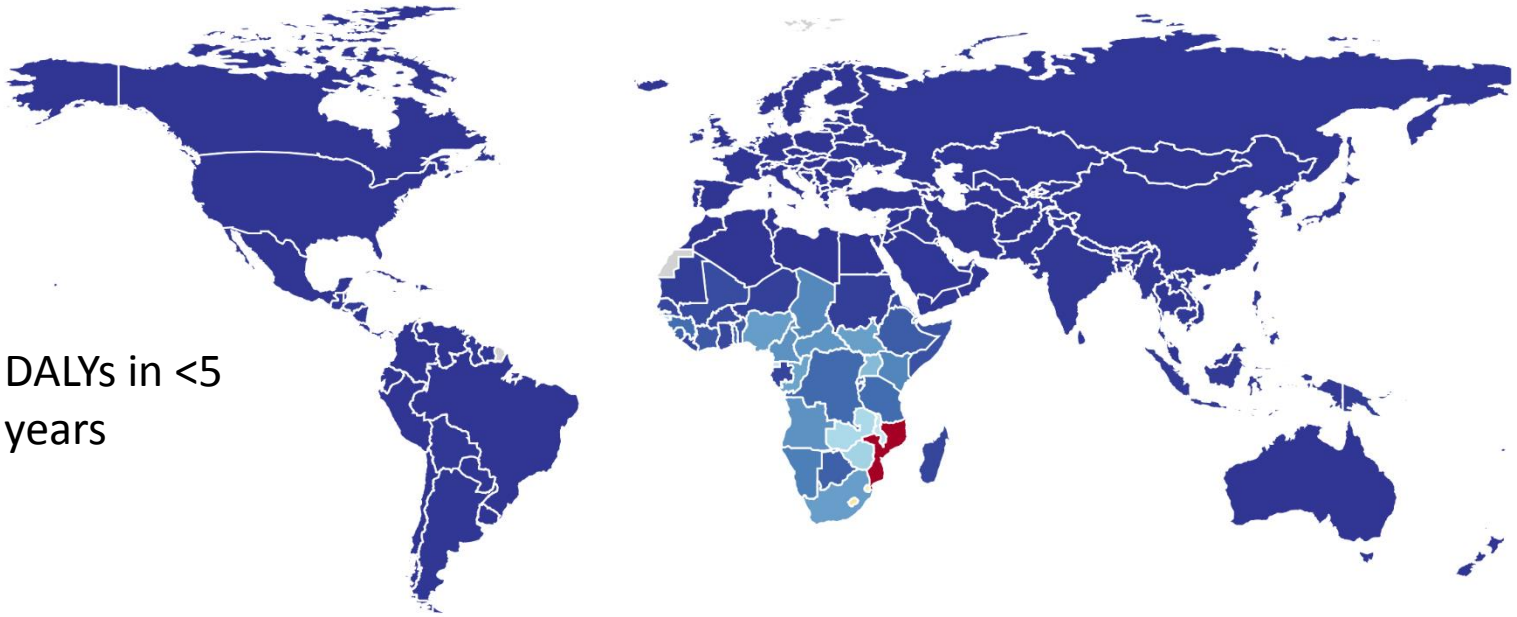


HIV/AIDS
Both sexes, All ages, 2013, DALYs per 100,000



DALYs in <5 years



DALYs in 5-14 years