



Neuroepidemiological issues in Africa *(sub-saharan Africa)*

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Inserm UMR 1094
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- ü Africa: a huge continent
- ü Methodological challenges
- ü Global burden of diseases
- ü Focus on some diseases
- ü Conclusion

The African continent

World's second-largest and second-most-populous continent

Area: 54 countries in 30 221 532 km²

Population:

1,075,615,883 (15% of World population)

829,000,000 in 48 Sub-Saharan countries

42 % < 15 yrs old

Life expectancy: 53 yrs

Infantile mortality rate: 85 %



Economy: GNP per capita: \$ 100 to 5,000 (RSA)
(vs \$ 65,000 Luxembourg)

Focus on sub-saharan Africa



Environment

- specific climate (tropical or sub-)
- resource-poor è poor sanitation/hygiene/housing
- specific environmental factors (*infections...*)

Means

- low access to health care with inequalities in geographic distribution
- poverty: limited health means
- low number of trained staff

Population

- specific sociocultural factors
- young with low life expectancy
- rapid, uncontrolled growth of urban centers
- inadequate health/sanitation facilities



“Political” issues

- rare stability
- few specific programs for neurological diseases
- health policy issues

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Methodological challenges

Definition of the population

Migrations

Sampling strategy: availability of census...

Validity of demographic data? (age....)

Refusals or subjects impossible to join



⇒ some solutions

- cluster sampling
- official documents...or specific methods (age: *time milestones*)
- sensitization of the local authorities and population
- well defined procedures +++

Methodological challenges

Ascertainment of cases

Difficulties in follow-up

Lack of trained specialists

Lack of neuroimaging devices (MRI, CT scan)

Operational difficulties

Ethnic diversity à many dialects and behaviours

Stigma...and then “hidden” cases?



⇒ some solutions

- use of multiple sources of information (\pm capture-recapture)
- use of standardized tools and definitions
- trained interviewers and interpreters
- make profit of demographic surveillance systems

Neuro Staff and means of diagnosis

One Neurologist for

250,000 people in the North and South (RSA)

600,000 to 6,000,000 people in the intertropical zone

Means of diagnosis

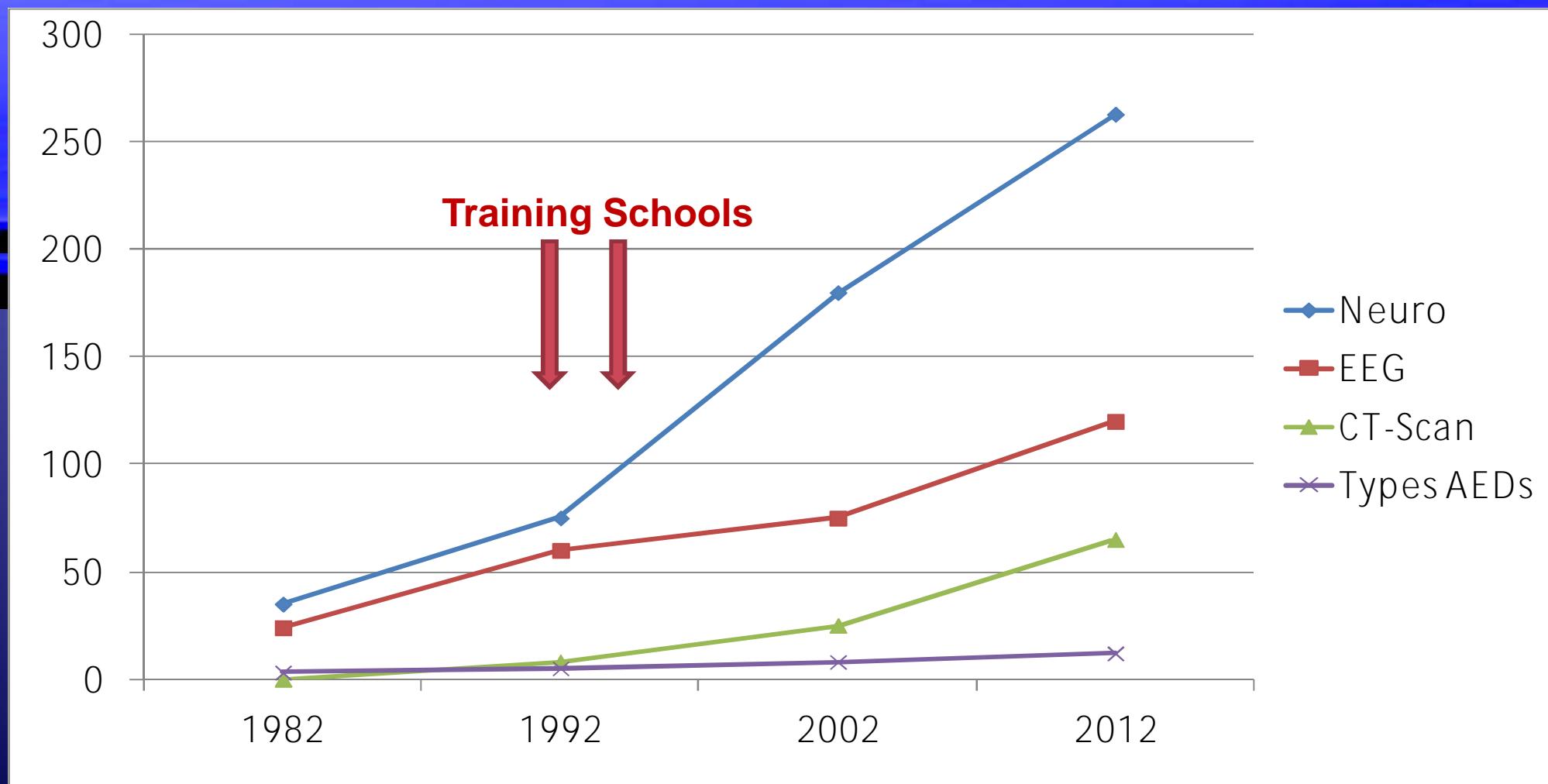
>200 EEG; >200 CT: for 205,000,000 North inhabitants

>150 EEG; >250 CT: for 60,000,000 South Afr. inhabitants

100-120 EEG; 70 CT: for 800,000,000 intertropical zone

Very limited number of MRI

Evolution of Neuro-Staff, EEG and AEDs 1982-2012 in Sub-Saharan Africa (excl. Maghreb and RSA)



Languages

In total, **3000 languages** are spoken in Africa
but 12 languages spoken by 75% of Africans

86 ethnic groups (with population > 10 million) in Africa

è *Importance of good translations and back-translations of the tools*

*Regardless of the difficulties,
standards of methodology should
be applied everywhere*

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THE GLOBAL BURDEN OF DISEASE: GENERATING EVIDENCE, GUIDING POLICY

SUB-SAHARAN AFRICA REGIONAL EDITION

INSTITUTE FOR HEALTH METRICS AND EVALUATION
UNIVERSITY OF WASHINGTON

HUMAN DEVELOPMENT NETWORK
THE WORLD BANK

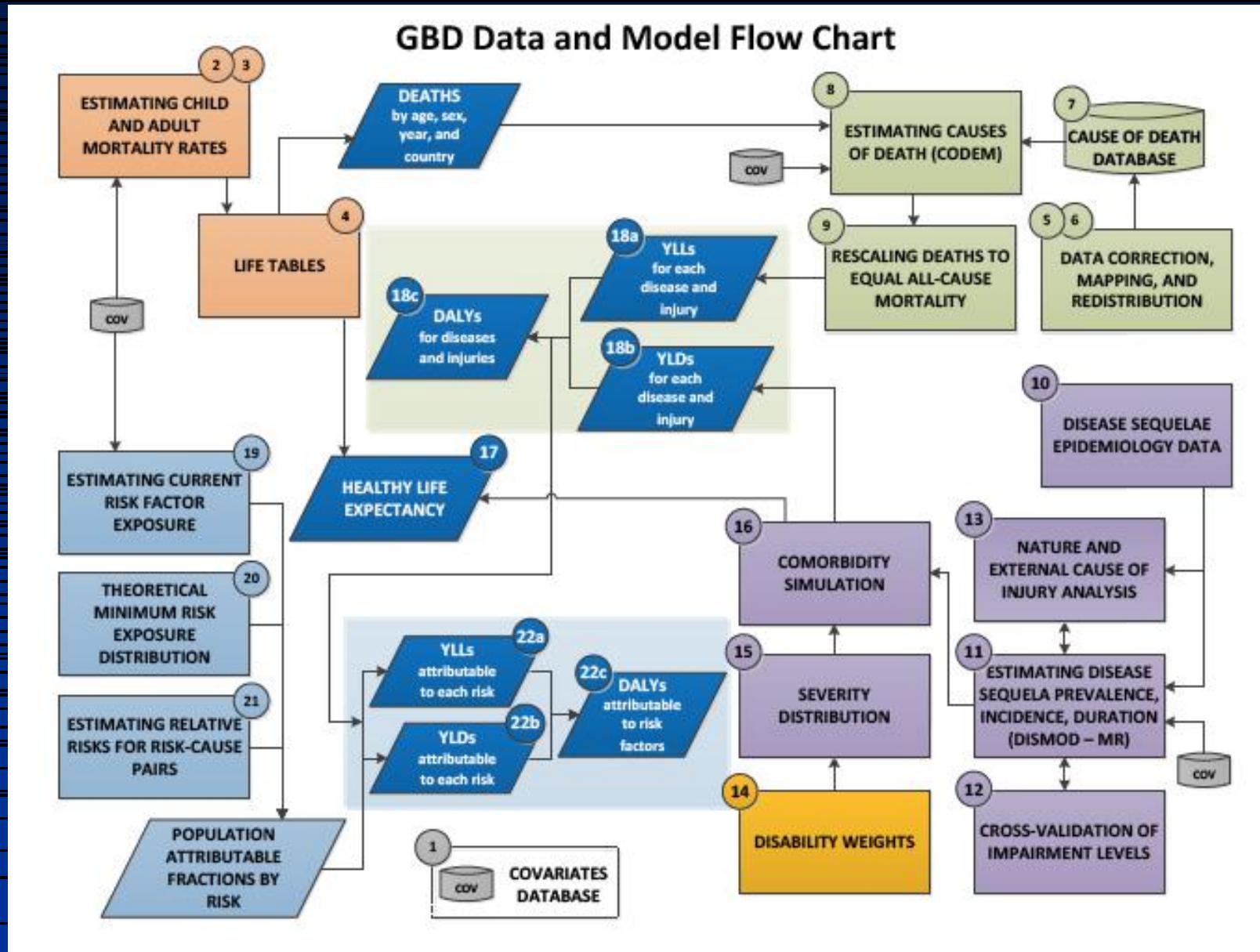
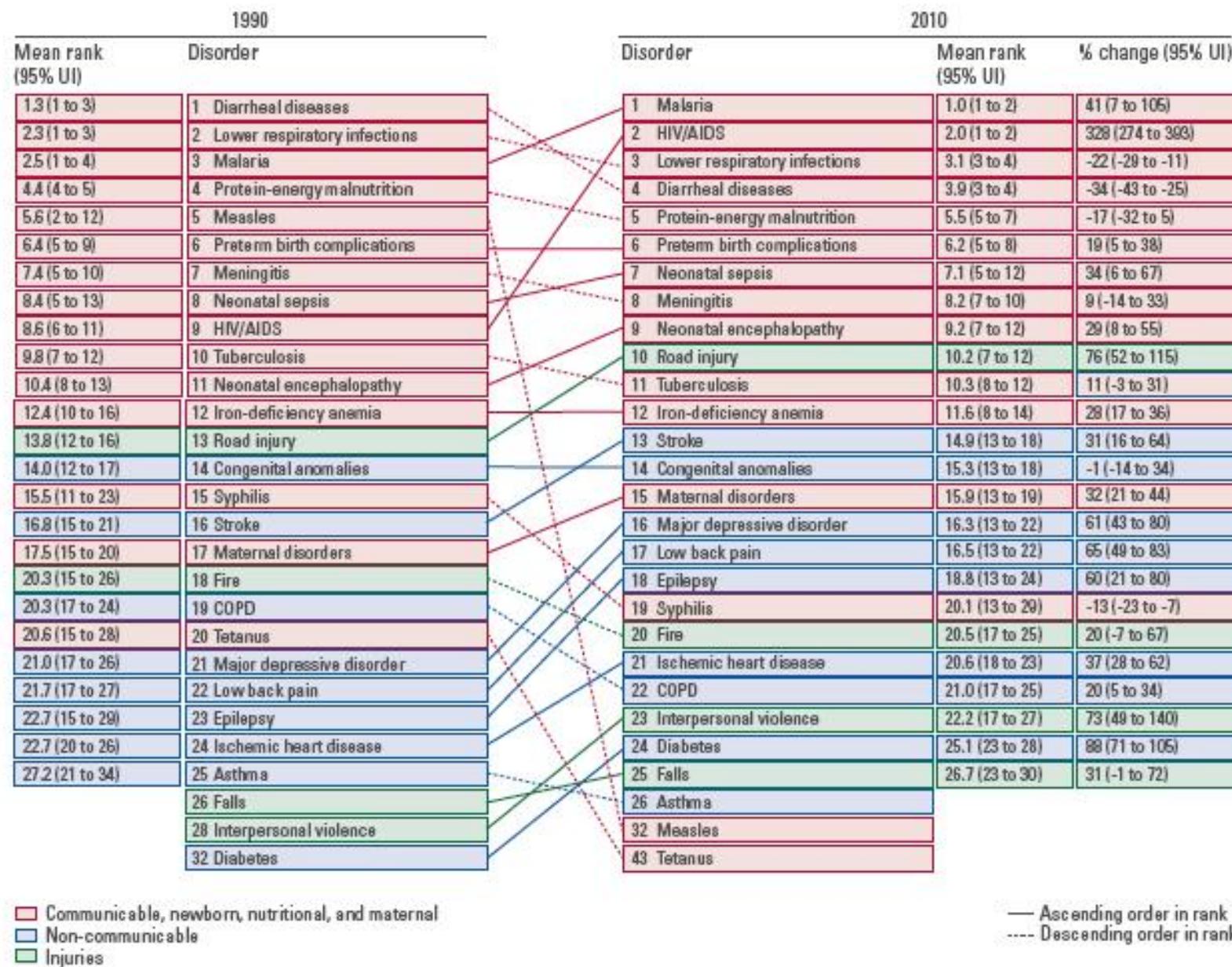
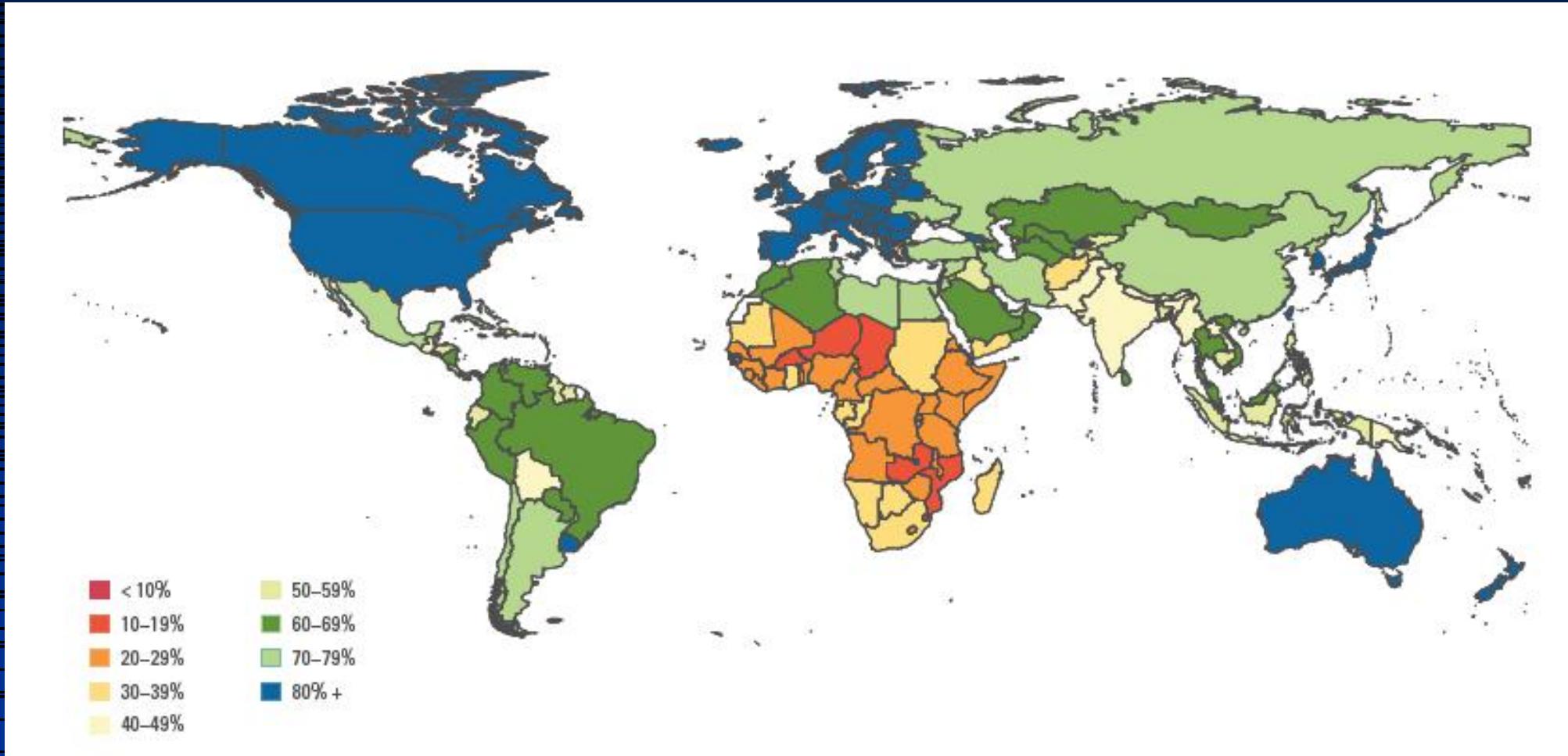


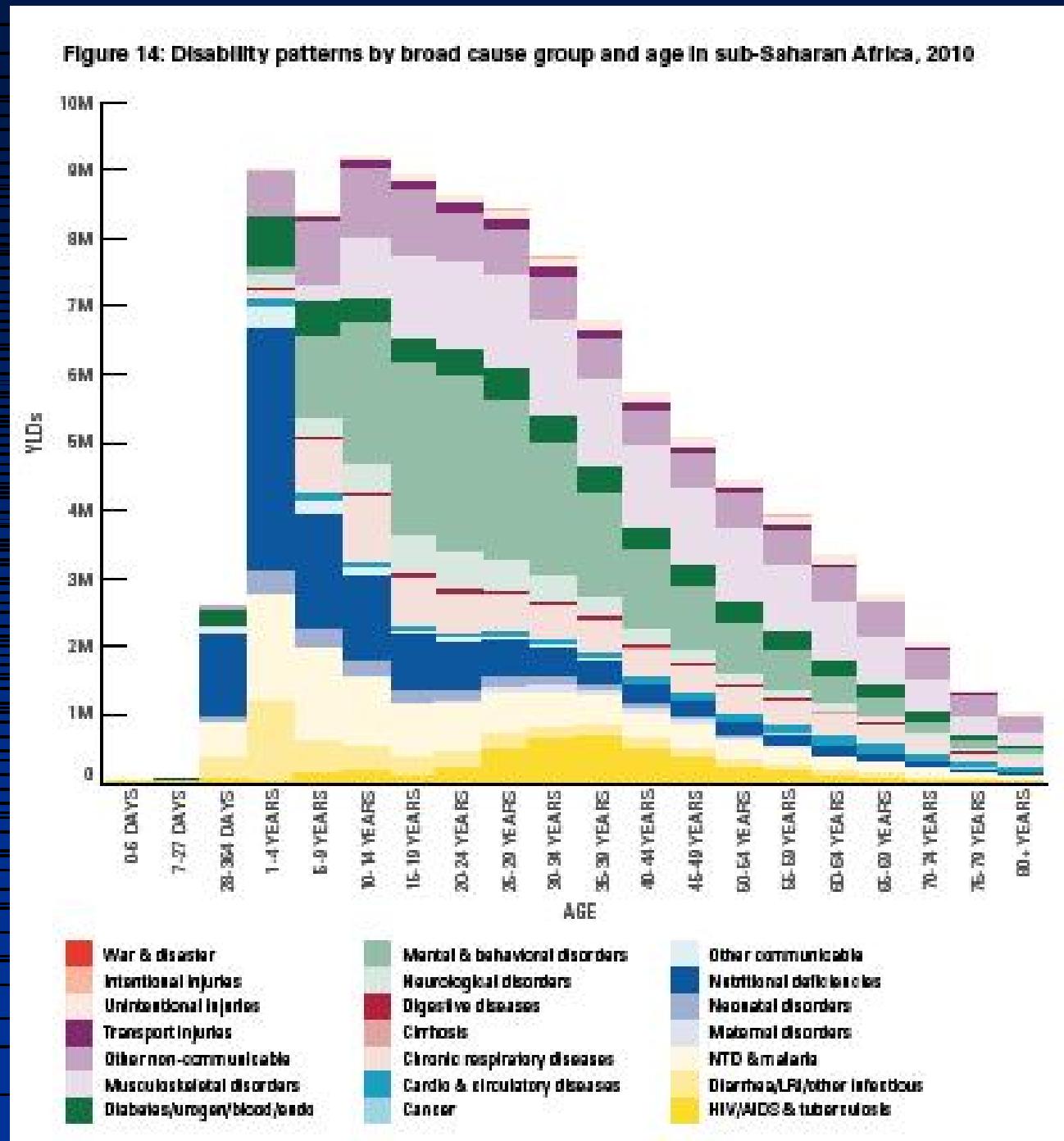
Figure 2: Disability-adjusted life year ranks, top 25 causes, and percentage change in sub-Saharan Africa, 1990-2010



Percentage of DALY due to NCD, GBD 2010



DALY, GBD, 2010



DALY, GBD, 2010

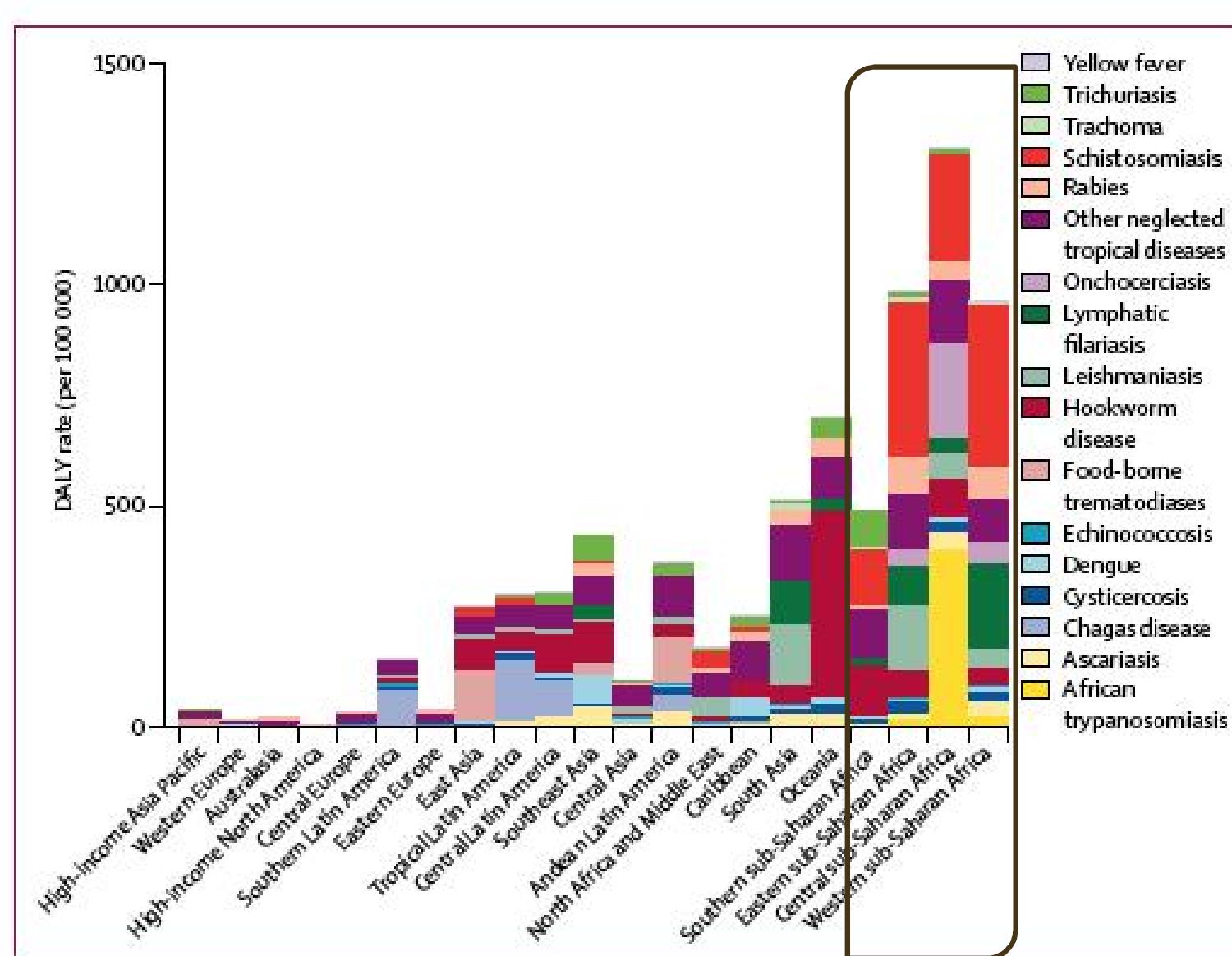
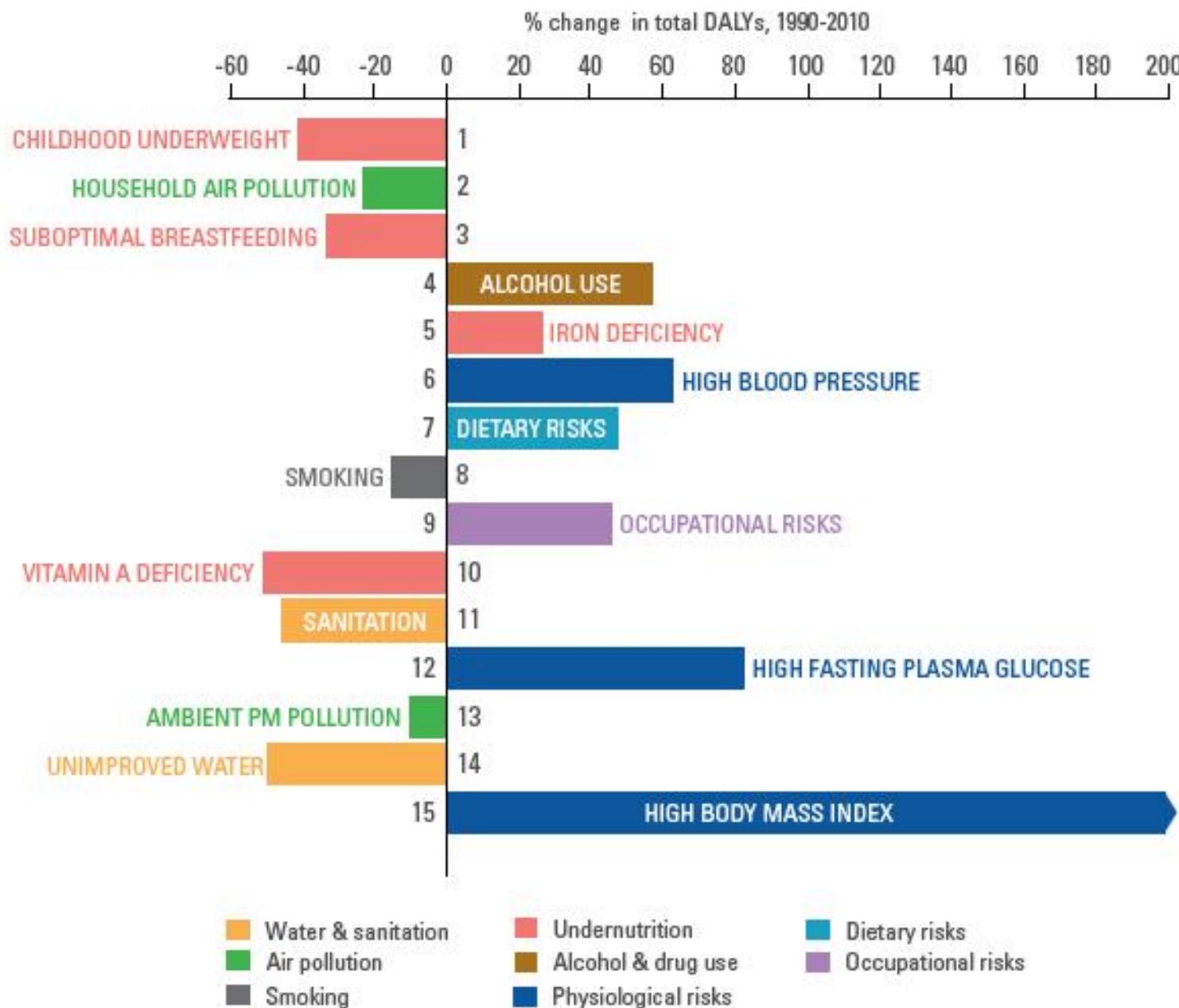


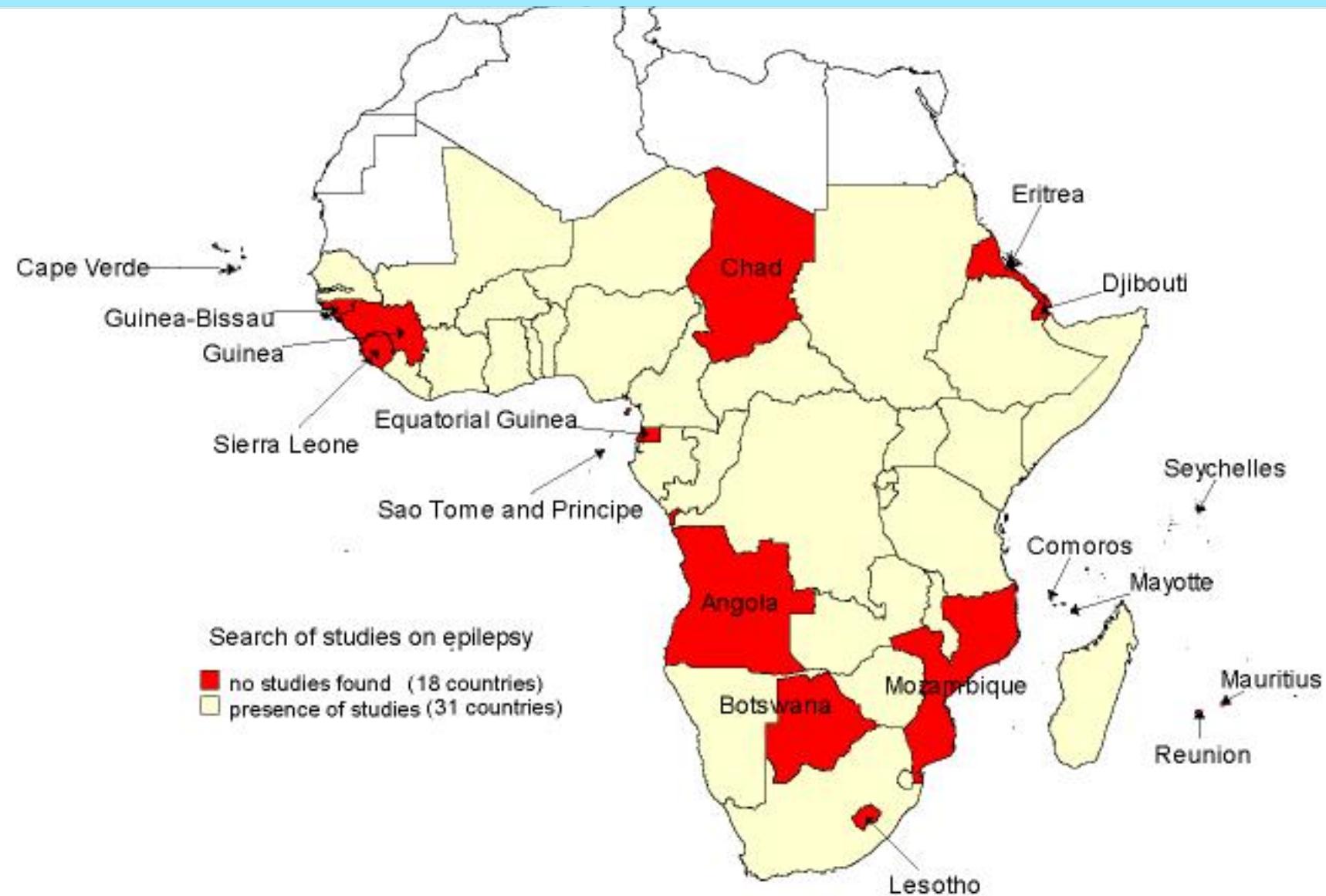
Figure 9: Neglected tropical disease disability-adjusted life year rates by cause and region in 2010
This figure excludes malaria.

Figure 17: Shifts in rankings of DALYs in sub-Saharan Africa for top 15 risk factors, 1990-2010



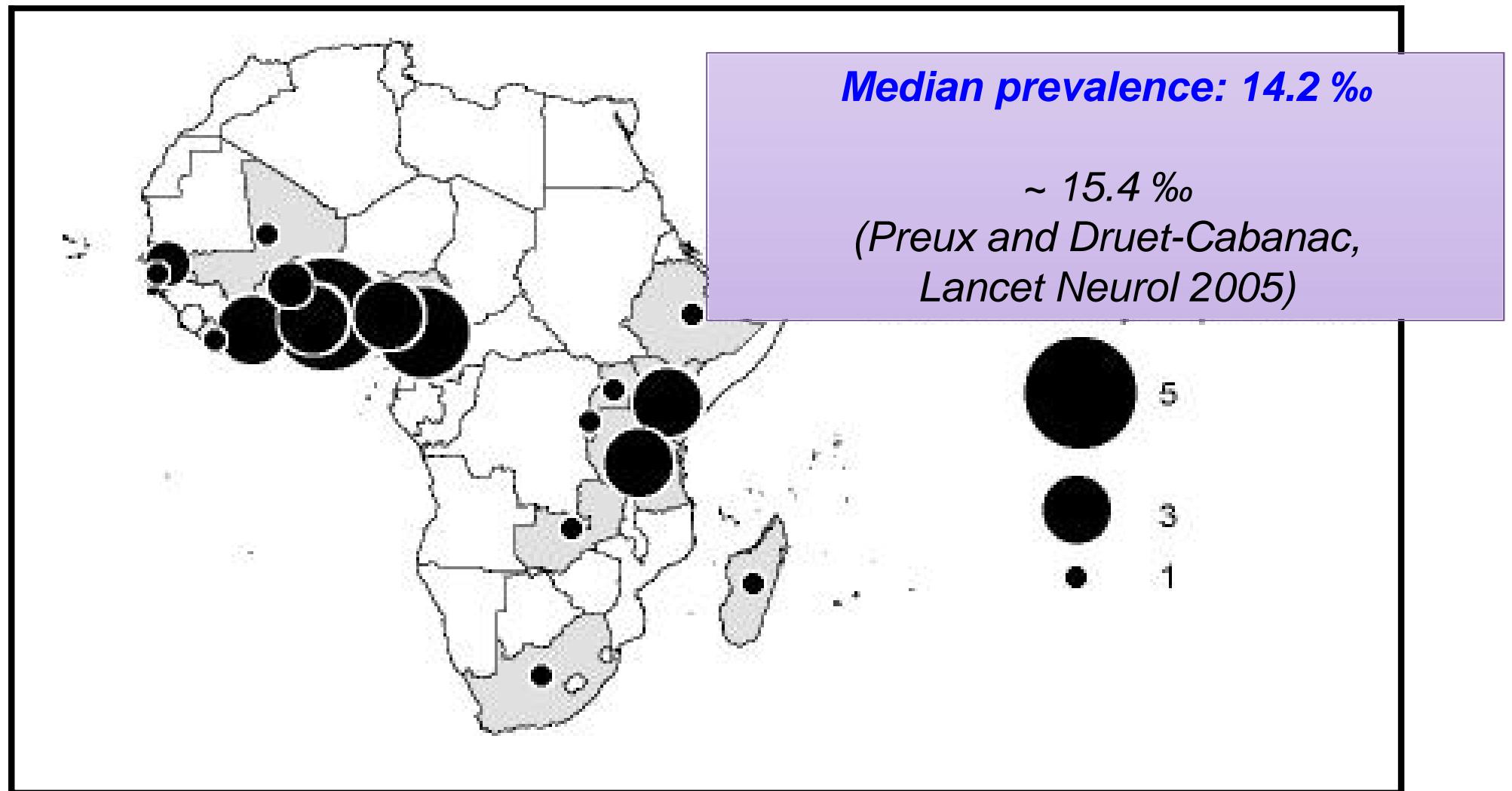
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No publication found in 18 (36%) countries!



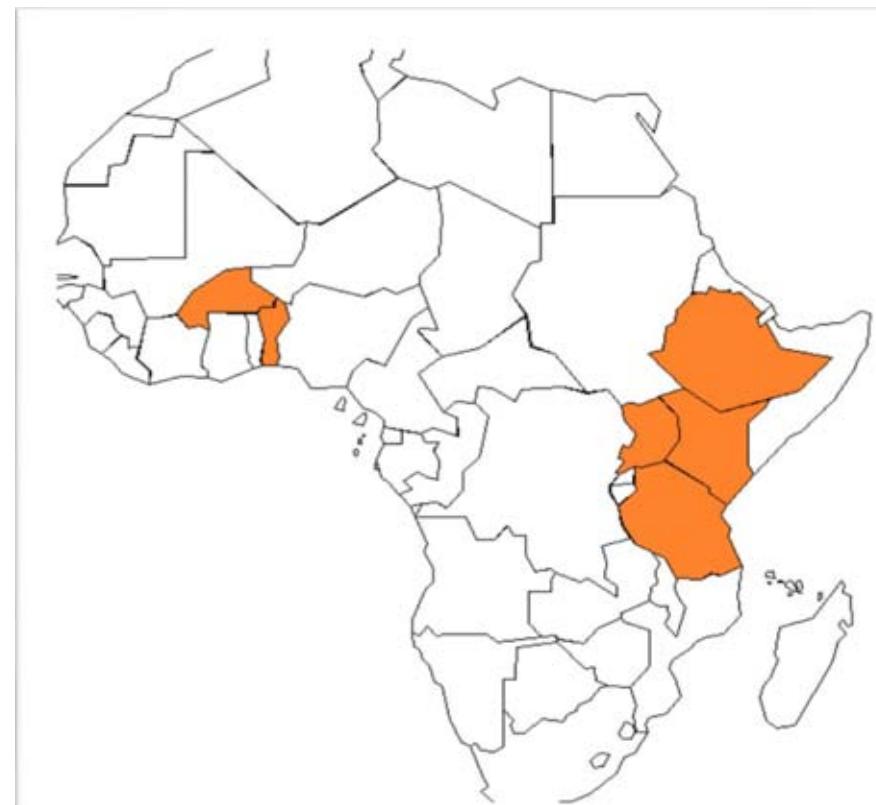
RECENT REVIEW OF EPILEPSY IN SUB-SAHARAN AFRICA

Number of study on epilepsy prevalence: 38 studies in Sub-Saharan Africa



Annual incidence (per 100 000)
only 7 estimates published in 6 countries

Ethiopia	64.0 (1997)
Benin	69.4 (2012)
Tanzania	73.3 (1992)
Tanzania	81.0 (2009)
Burkina Faso	83.0 (1993)
Uganda	156.0 (1998)
Kenya	187.0 (2008)





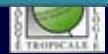
Risk factors

Very few well-conducted analytical studies exist, in particular case-control studies or (historical) cohort studies...

Problems: only prevalence cases, not representative, too few controls, no neuroimaging, all the potential risk factors not studied, no information on the latency between the first acute symptomatic seizure and the onset of epilepsy ...

Countries	Year	N Epilepsy cases	N Controls	Multivariate analysis	OR Febrile seizures	OR familial history	OR head trauma	OR perinatal disorder	OR prior infection	OR Parasitosis onchocerciasis	OR Parasitosis cysticercosis
Nigeria	1989	155	155	No	11.0		13.0				
Burundi	1997	103	72	No							4.6
Burundi	1997	110	82	No							1.4
CAR	1999	187	374	No						NS	NS
Mali	2000	70	140	No						NS	NS
Tanzania	2001	174	174	Yes	2.9	3.6		4.5	3.8		
Burundi	2003	324	648	Yes		3.3		1.9			4.1

Case-control studies in subsaharan Africa; OR: odds ratio; NS: factor studied but not significant



Cysticercosis

Infestation by the larval form of *Taenia solium*

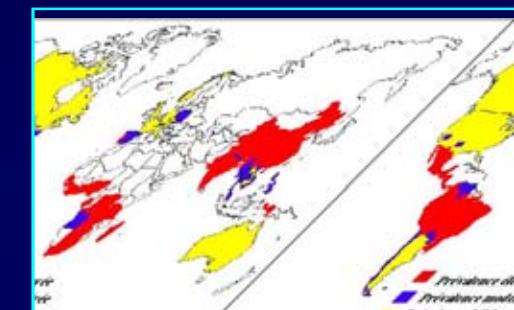
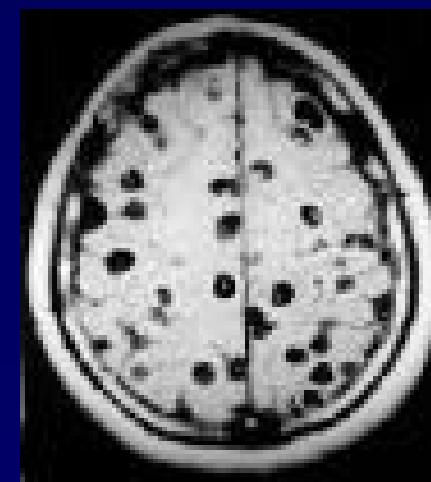
Pork = intermediate host

Encystation in the central nervous system

Very frequent acute seizures (~50%; up to 92%!)

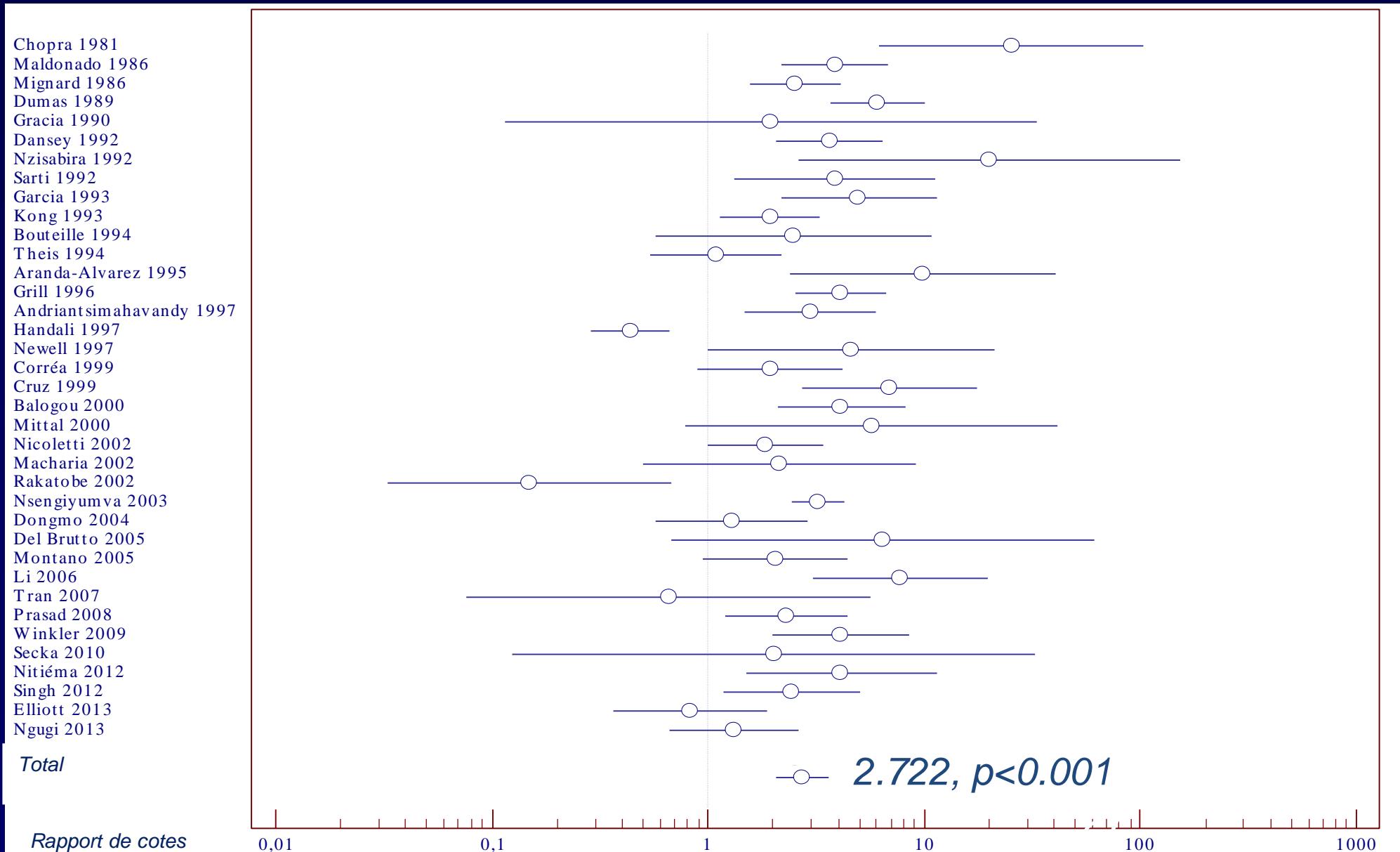


First cause of late-onset epilepsy in endemic areas?





Debacq et Preux, personal data

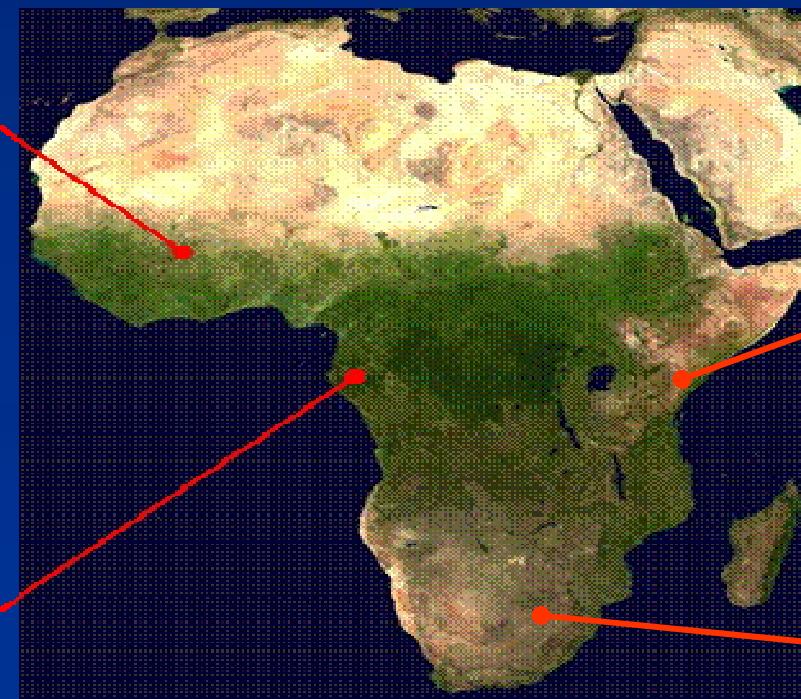


Cerebral malaria

Several recent epidemiological studies in sub-Saharan Africa



Ngoungou et al.,
Epilepsia 2006; 47:2147-53.



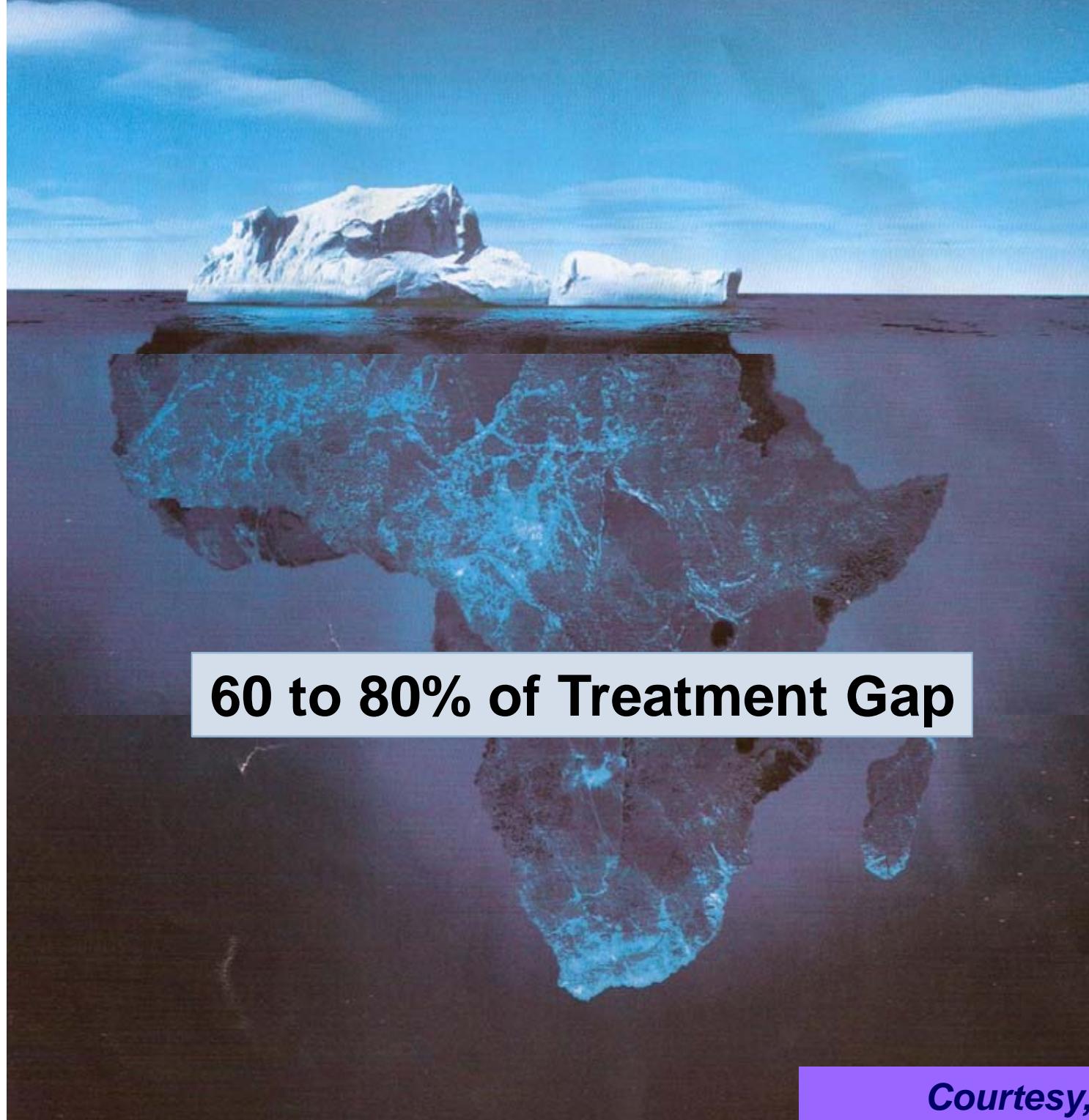
Ngoungou et al.,
Epilepsia 2006; 47: 873-9.



Carter et al.,
Epilepsia 2004; 45: 978-81.



Birbeck et al.,
Lancet Neurol 2010; 9: 1173-81.



Courtesy, AG Diop

Causes of treatment gap

Causes of a « diagnostic » treatment gap

Mistakes

No paraclinical examinations or trained staff

No access to health system (distance and/or cost)

Deny of the disease

Misbeliefs

Causes of the treatment gap

No availability of the drug(s)

No money to buy the drug(s)

Low quality of the drug(s)

Prescription mistake

Choice to undergo only a traditional treatment



Cultural context



- ? áSupernatural (punishment)
- ? áDevil action or “bad eyes”
- ? áUntreatable
- ? áContagious:
 - saliva, blood, sweat, urines, breath
 - breast feeding
 - chicken feces
 - contact with dogs...

Very severe prognosis

- high frequency of seizures
(> 90% active epilepsies)

- injuries, drownings, burns into open fire
- status epilepticus
- undernutrition
- high mortality



Burundese girl burned

Prevalence and incidence of stroke in Africa

Prevalence studies

- South Africa: 300 / 100,000
- Tanzania: 200 / 100,000
- Nigeria: 114 / 100,000
- Nigeria: 58 / 100,000

Incidence-studies

- Nigeria: 15 / 100,000 / yr
- Zimbabwe: 30 / 100,000 / yr

Prevalence of stroke in Cotonou, Benin

Age group years	Total population		Males		Females	
	stroke prevalence n/1,000	number of strokes/ population size	stroke prevalence n/1,000	number of strokes/ population size	stroke prevalence n/1,000	number of strokes/ population size
15–44	0.3	4/12,580	0.6	3/5,300	0.1	1/7,279
45–54	14.0	17/1,212	20.3	9/443	10.4	8/769
55–64	23.8	19/799	29.1	9/309	20.4	10/490
65–74	51.7	18/348	62.9	10/159	42.3	8/189
75–84	74.6	10/134	120.0	6/50	74.1	4/84
85+	66.7	2/30	111.1	1/9	47.6	1/21
Total	4.6	70/15,103*	6.1	38/6,270	3.6	32/8,832

* Total population: 15,155; population size by age: 15,103, with 52 missing.

Incidence of ischemic cardiopathies and stroke in East Africa

Model parameter	Disease incidence (per 1000 population)	Age groups in AfrE (years)				
		30–44	45–59	60–69	70–79	≥80
Ischaemic heart disease	Men	0.31	2.08	4.55	6.02	8.20
	Women	0.14	1.02	2.53	3.34	4.72
Cerebrovascular disease	Men	0.87	2.93	6.86	13.0	20.1
	Women	0.91	3.33	5.74	12.3	22.5

Stroke mortality rates

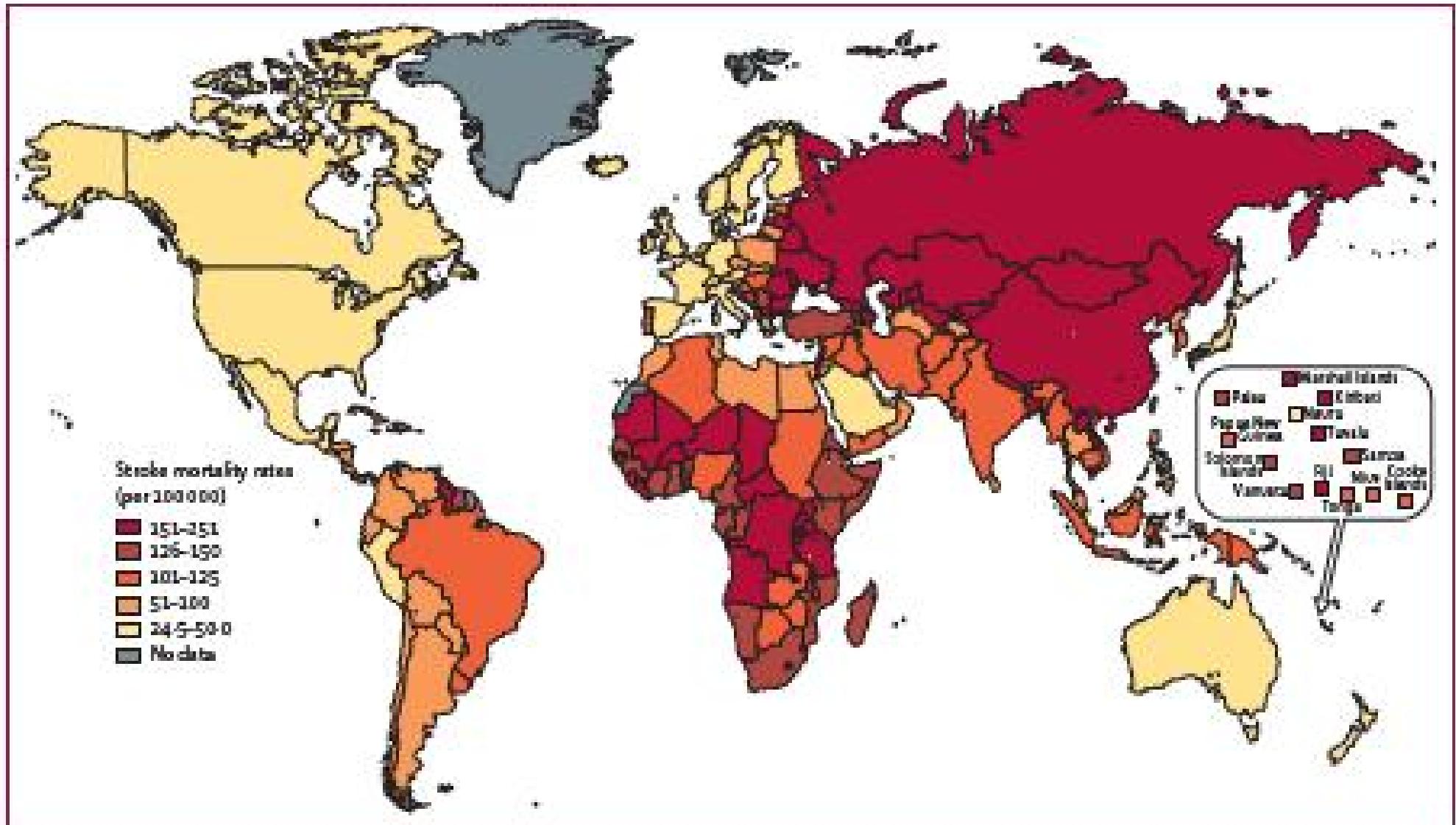


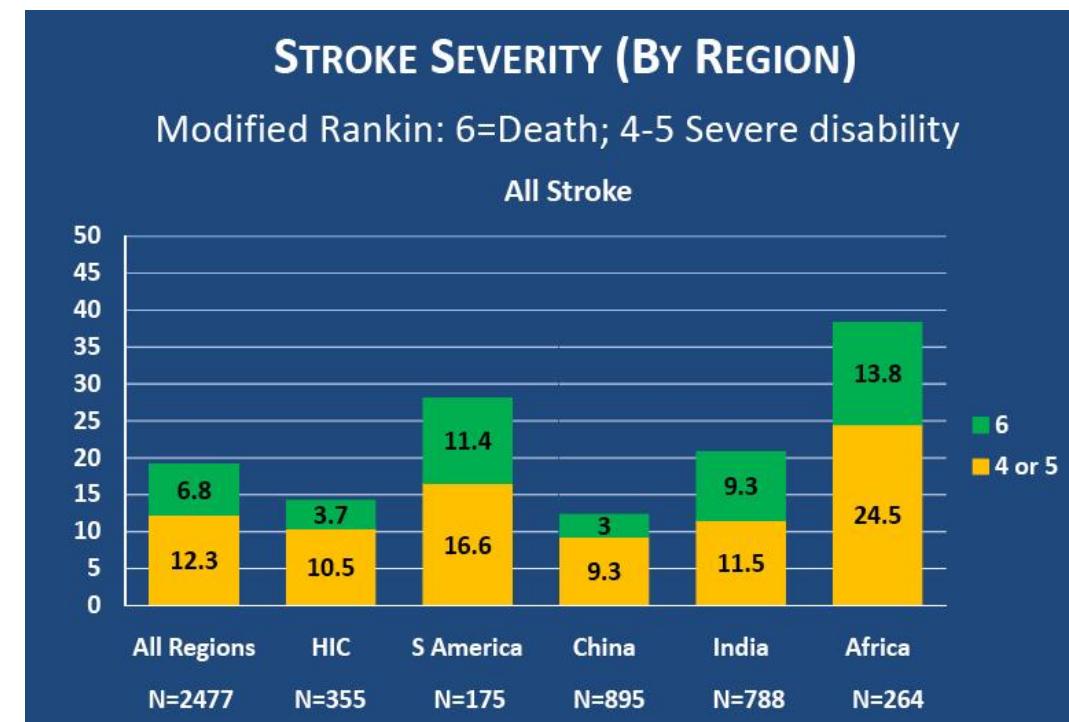
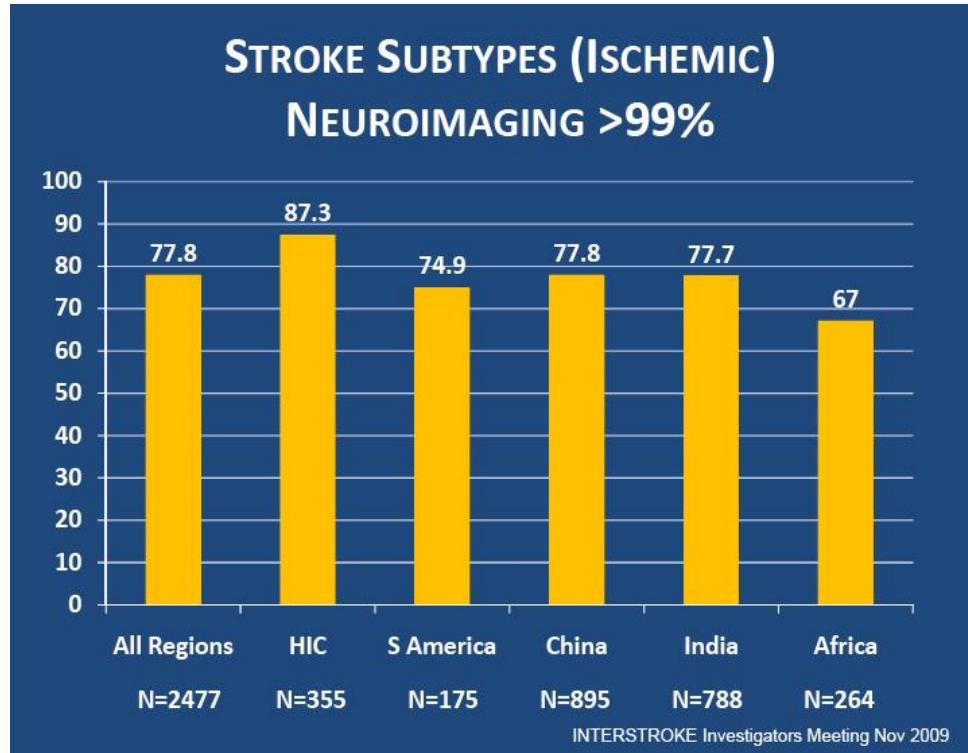
Figure 1: Age-adjusted and sex-adjusted stroke mortality rates
Rates are highest in eastern Europe, north Asia, central Africa, and the south Pacific.

Johnston et al., 2009

Mortality from stroke, compared to myocardial infarction

Countries	Mortality / stroke per 100 000 / yr (% of global mortality)	Mortality / myocardial infarction per 100 000 / yr (% of global mortality)
Benin	143 (8.8)	113 (7.0)
Senegal	143 (9.2)	120 (7.7)
Congo	123 (7.8)	102 (6.5)
Gabon	120 (8.5)	103 (7.2)
France	28 (6.1)	38 (8.3)

- Africa
 - ▶ Mozambique, Nigeria, South Africa, Sudan, Uganda



Neurology®

Stroke in Sub-Saharan Africa: An Urgent Call For Prevention

Jerome H. Chin

Neurology 2012;78:1007-1008

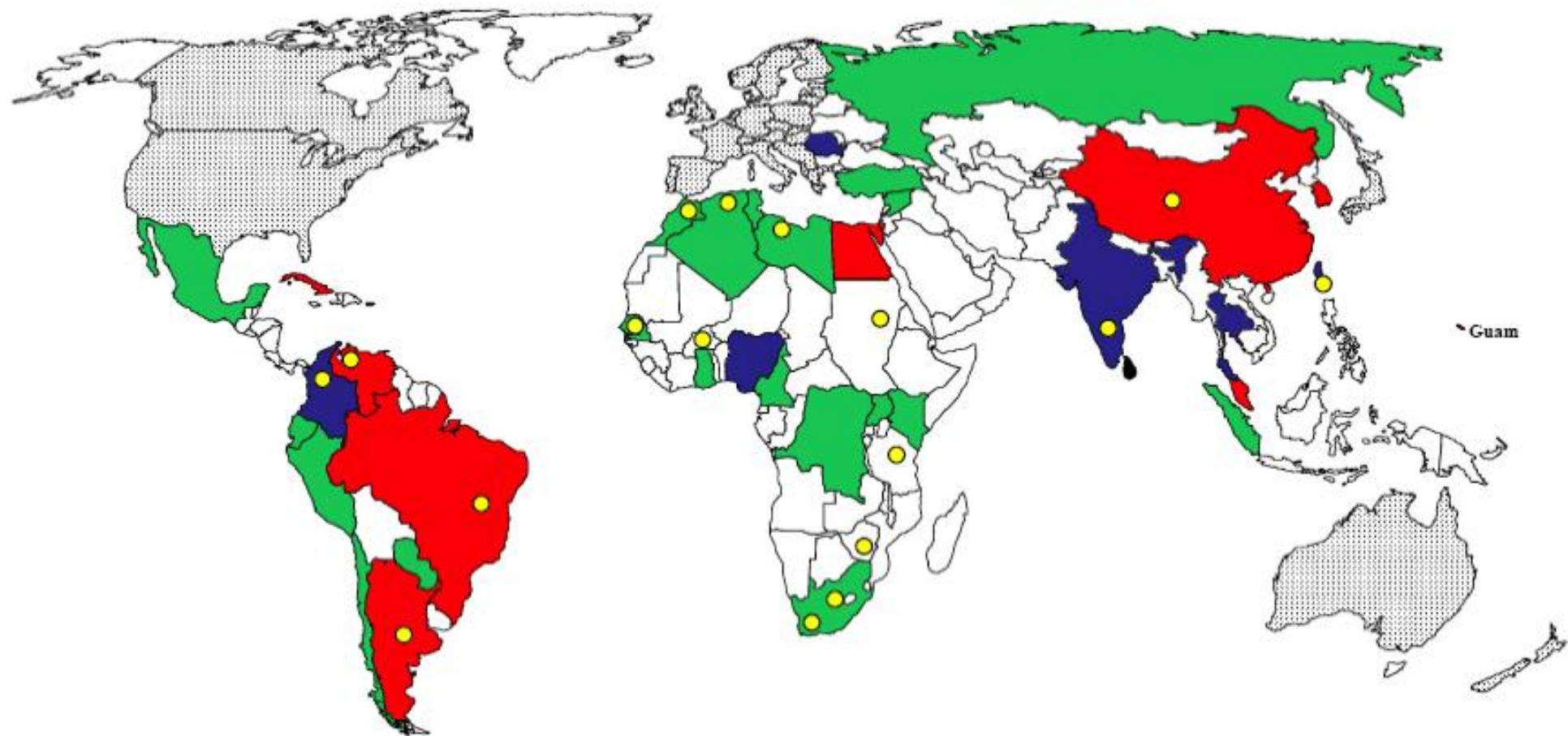
DOI 10.1212/WNL.0b013e318248df95

NIGERIA : Ibadan / USA : Indianapolis Dementia Project

Ethnic group: Yorubas, + de 65 ans

Prevalences	Dementia	AD
Ibadan, Nigeria	2.3%	1.4%
Indianapolis, USA	8.2%	6.2%

Dementia



- Prevalence or incidence comparable to developed countries
- Associated factors studied but no prevalence data
- Low prevalence <3%
- Clinical cases reported

Africa

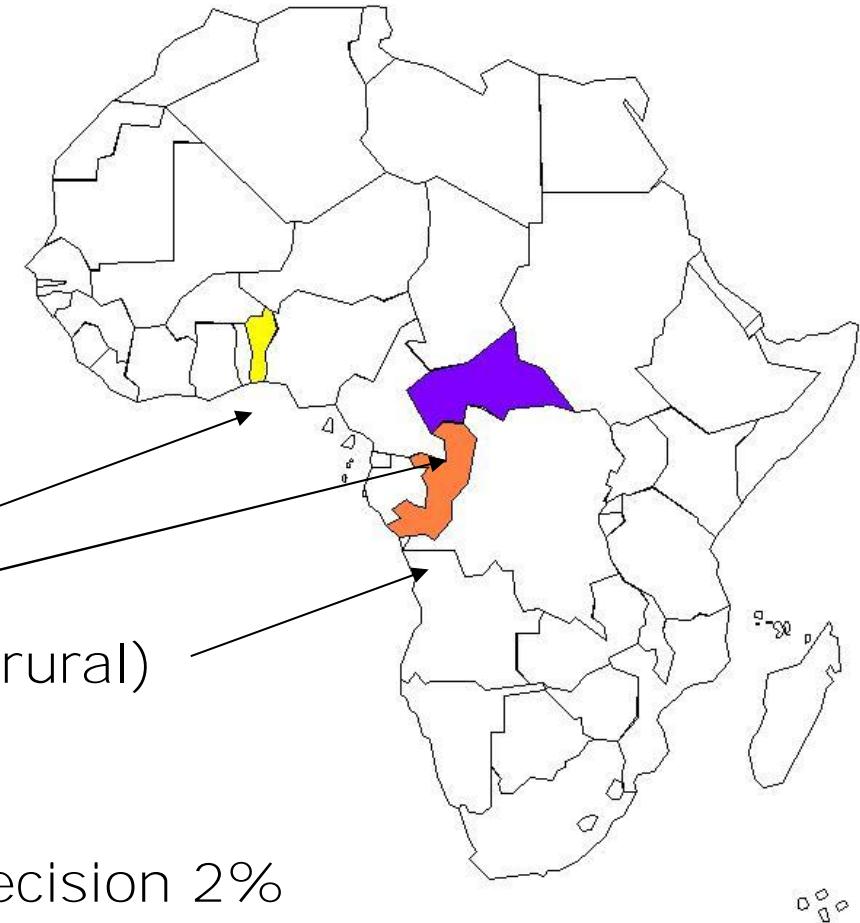
Countries		Prevalence of dementia (% & CI 95%)
Mali	Bamako (<i>Traoré et al., 2002</i>)	AD = 1.2
	Koulikouro (<i>Gunito et al., 2004</i>)	AD possible = 1.8 AD probable = 6.6
Nigeria	Ibadan (<i>Hendrie et al., 1995</i>)	2.3 (1.2-3.4)
	Jos (<i>Ochayi et al., 2006</i>)	6.4 (3.8-9.9)
Tanzania (<i>Longdon et al., 2012</i>)		?>70 yrs: 6.4 (4.9-7.9)

Our studies in SSA (IENT, UMR1094 NET, Limoges)

Benin, CAR, Congo

- Cross-sectional DTD population-based surveys
?z65 yrs
- Locations:
 - ü Benin: Cotonou (urban), Djidja (rural)
 - ü CAR: Bangui (urban), Nola (rural)
 - ü Congo: Brazzaville (urban), Gamboma (rural)
- Number of needed subjects:

Based on expected prevalence 5%; precision 2%
= 456 subjects ?-65 yrs
è 500 subjects per site



Funded by
French Ministry of Foreign Affairs
French National agency for research,
AXA Research fund

Our results (I ENT, UMR1094 NET, Limoges)



Countries		Crude prevalence of dementia (CI 95%)	Crude prevalence of AD (CI 95%) (% AD in dementia)
Benin	Djidja (<i>Guerchet et al., 2009</i>)	2.6 (1.1-3.8)	2.2 (1.1-3.9) (84.6%)
	Cotonou (<i>Paraiso et al., 2011</i>)	3.7 (2.6-4.8)	2.8 (1.9-3.9) (75.7%)
CAR	Bangui EDAC (<i>Guerchet et al., 2010</i>)	8.1 (5.8-10.8)	6.6 (4.6-9.2) (81.4%)
	Bangui ANR Epidemca*	6.4 (4.4-8.9)	4.4 (2.8-6.6) (68.7%)
	Nola ANR Epidemca*	8.5 (6.1-11.3)	7.8 (5.6-10.6) (91.7%)
Congo	Brazzaville EDAC (<i>Guerchet et al., 2010</i>)	6.7 (4.7-9.2)	4.6 (3.0-6.8) (68.6%)
	Brazzaville ANR Epidemca*	6.6 (4.6-9.0)	4.2 (2.6-6.3) (63.6%)
	Gamboma ANR Epidemca*	5.7 (3.8-8.0)	4.3 (2.8-6.4) (75.4%)

* UMR1094, data 2013, not published

Mortality – Central Africa

- 93.4% of subjects followed-up (n=371/397)
- **Mortality after 2 yrs of follow-up:**

	Dementia (n=75)	p	CIND (n=222)	p	Controls (n=105)
Bangui	32.5% [CI95% : 18.6-49.1]	<i>p=0.016</i>	12.1% [CI95% : 6.9-19.2]	<i>p=0.486</i>	16.4% [CI95% : 8.1-28.1]
Brazzaville	40.0% [CI95% : 23.9-57.9]	<i>p=0.009</i>	13.3% [CI95% : 7.2-21.6]	<i>p=0.467</i>	6.8% [CI95% : 1.4-18.6]

Dementia vs Controls: Bangui: p=0.059 / Brazzaville: p=0.004

No difference between towns

Genetic factors in dementia in SSA: ApoE, no link??

Benin (*Guerchet et al., 2009*)

- ü No influence of ApoE epsilon 4
- ü ApoE epsilon 2: OR=0.12 (CI95%=[0.02-0.89]), p=0.038

Kenya (*Chen et al., 2010*)

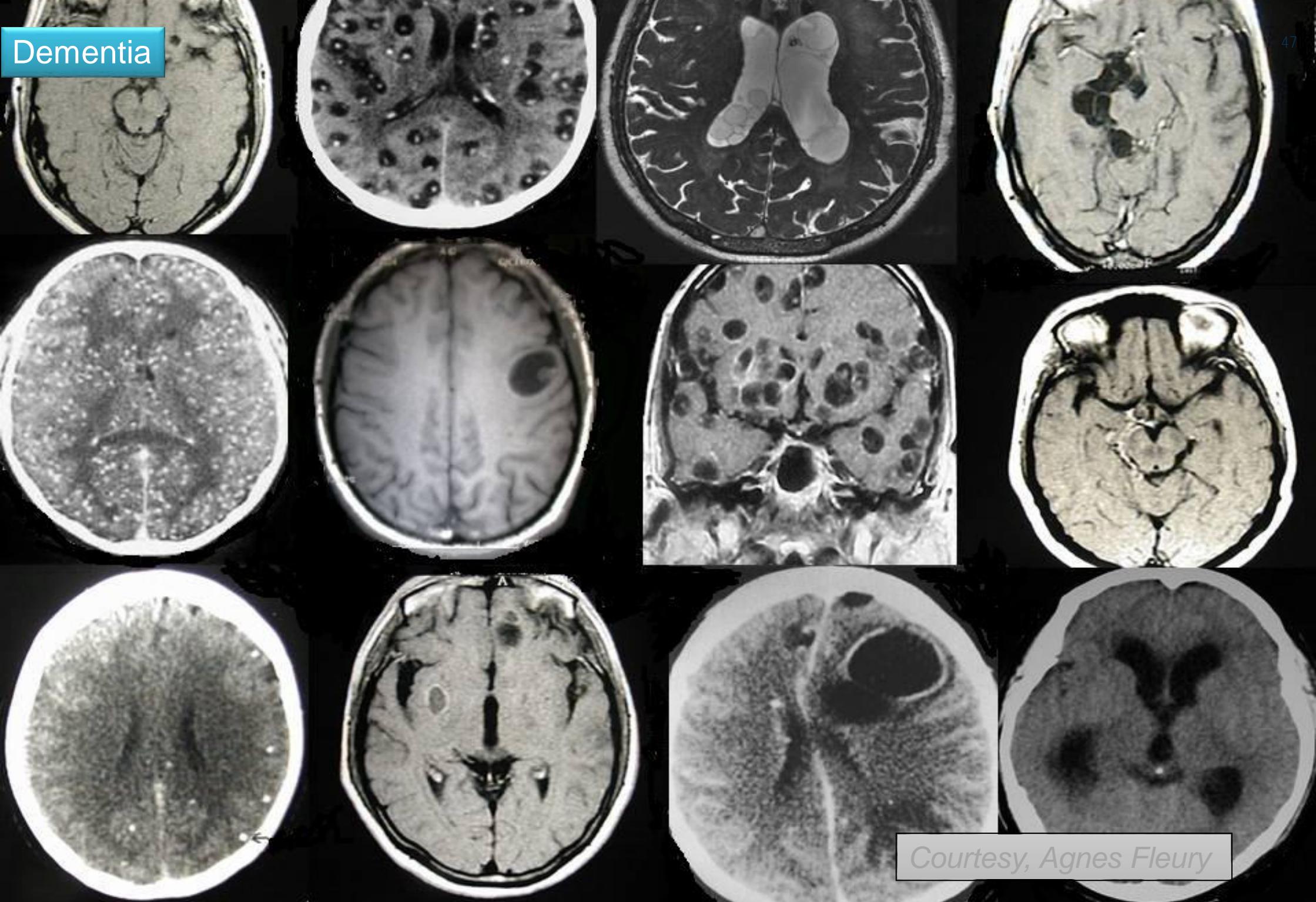
Nigeria (*Gureje et al., 2006 ; Hall et al., 2006*)

Tanzania (*Sayi et al., 1997*)

- ü No influence of ApoE epsilon 4

Dementia

47



Courtesy, Agnes Fleury

Parkinson Disease

Only few community – based studies (*Ethiopia, Nigeria, Tanzania, Togo*):

Movement Disorders
Vol. 21, No. 12, 2006, pp. 2150–2156
© 2006 Movement Disorder Society

Parkinson's Disease in Africa: A Systematic Review of Epidemiologic and Genetic Studies

Njideka U. Okubadejo, MD,^{1,2} James H. Bower, MD,^{1,*} Walter A. Rocca, MD, MPH,^{1,3} and Demetrius M. Maraganore, MD¹

TABLE 2. *Prevalence studies of Parkinsonism and Parkinson's disease in Africa*

Country ^a	Year (study duration)	Population size	Crude prevalence ^b (per 100,000)	Prevalence in specified age range ^b	Diagnostic criteria or protocol
Nigeria ^{27,28}	1982 (1.5 yr)	20,000	10	59 (> 39 yr)	WHO protocol and three of four cardinal signs
Libya ²⁹	1982 (~ 2 yr)	518,745	31.4	285.1 (> 50 yr)	Two of 4 cardinal signs; no exclusion criteria
Tunisia ³⁰	1985 (~1 month) ^d	34,874	43	216 (≥ 40 yr) 296 (≥ 50 yr)	WHO protocol ^c
Ethiopia ³¹	1986 (~2 yr)	60,820	7	—	Not detailed
Togo ³²	1989	19,241	20	—	WHO protocol ^c
	1995	4,182	20	—	WHO protocol ^c

Parkinson Disease

The Prevalence of Parkinson's Disease in Rural Tanzania

Catherine Dotchin,^{1*} Olivia Msuya,² John Kissima,³ John Massawe,³ Ali Mhina,³ Addess Moshi,³ Eric Aris,⁴ Ahmed Jusabani,⁵ David Whiting,⁶ Gabriel Masuki,³ and Richard Walker¹

n = 161,071

Prevalence: 20/100 000

Prevalence std: 40/100 000

**Parkinsonism in a population of northern Tanzania:
a community-based door-to-door study in combination
with a prospective hospital-based evaluation**

Andrea Sylvia Winkler · Esra Tütüncü ·
Anna Trendafilova · Michael Meindl ·
John Kaaya · Erich Schmutzhard · Jan Kassubek

n=1569 ? 50 yrs

Prevalence: 0??

'We call it the shaking illness': perceptions and
experiences of Parkinson's disease in rural
northern Tanzania

Gerry Mshana^{1*}, Catherine L Dotchin² and Richard W Walker³

Migraine

Some prevalence studies in Africa

Table 4 Some migraine prevalence studies among populations

Year	Authors (references)	Country	Migraine definition	Timeline	Population	Age of interviewees, years	Prevalence		Overall prevalence, %
							M	F	
1982	Osuntokun et al. (10)	Nigeria	AHC	–	Rural community	All	4.6	8.8	6.7
1983	Levy (23)	Zimbabwe	AHC	1 year	Rural community	>5	3.5	8.9	4.2
1984	Ogunyemi (18)	Nigeria	AHC	Whole life	Students	16–42	15.6	19.8	16.7
1988	Longe and Osuntokun (24)	Nigeria	–	–	Rural community	All			6.3
1992	Osuntokun et al. (11)	Nigeria	AHC	–	Urban community	All	5.0	5.6	5.3
1993	Romdhane Attia et al. (25)	Turisia	–	–	–	0–100	2.5	4.5	3.4
1995	Matuja et al. (26)	Tanzania	AHC	2 years	Urban community	20–40	–		7.2
1995	Tekle-Haimanot et al. (9)	Ethiopia	IHS	1 year	Rural community	>20	1.7	4.2	3.0
2004	Dent et al. (8)	Tanzania	IHS	1 year	Rural community	>11	2.5	7.0	5.0
2003	Our Study	Benin	IHS	Lifetime	Rural community	>15	2.2	4.0	3.3

Perfect illustration of wide methodological variations in data collection, criteria, timelines, populations...

Example of a rare disease: ALS

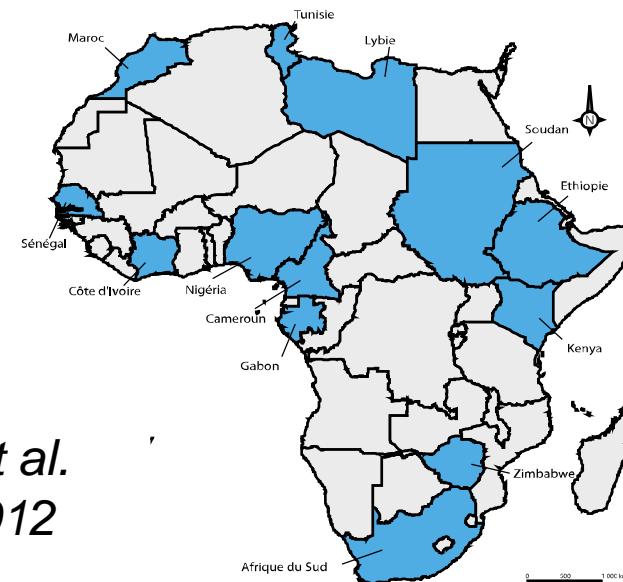
✓ Literature review

Ø 35 studies - ALS in Africans

- 21 performed in Africa
- 14 migration studies

Ø Characteristics of ALS

- Younger age at onset: 50 years
- Existence of juvenile forms
- Median SR: 2.75



Marin et al.
ALS, 2012

Problems of the availability of data for population-based estimates

✓ TROPALS study (n=44)

- Mean age: 52 years
- 1 case<25y; 2 cases<30y
- SR: 2.60



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Conclusions



- Methodological challenges
- Too few well-conducted studies
- Realities vary regions to regions, or countries to countries, and sometimes even within the same countries, depending for example of the risk factors
- Progression of neurological and mental health disorders in terms of DALY and deaths

**Neuroepidemiological studies in Africa are now
not only a necessity**

but an emergency...

What can be done ?

1. Improve and stimulate training by research
2. Propose methodological support
3. Approach global funding and stakeholders
4. Increase number of studies

1. Improve and stimulate training by research

Master + PhD

MASTER

Neuroépidémiologie et Parasitologie Tropicales

As an example : **Master Degree in Tropical Neuroepidemiology and Parasitology, Limoges, France**

- **PhD in cotutorship +++**
- **Intensive courses in Africa in Neuroepidemiology (initiatives exist)**
- **International organizations could play a role**

2. Propose methodological support

Create or develop methodological Units

- Sub-regional or regional first
- In each country in a second time

True technical plate-forms

**with skills in creating databases,
data-management, biostatistics
with professional softwares**

HUMAN RESOURCES



**= one of the keys towards publications
in higher level journals**

3. Approach global funding and stakeholders

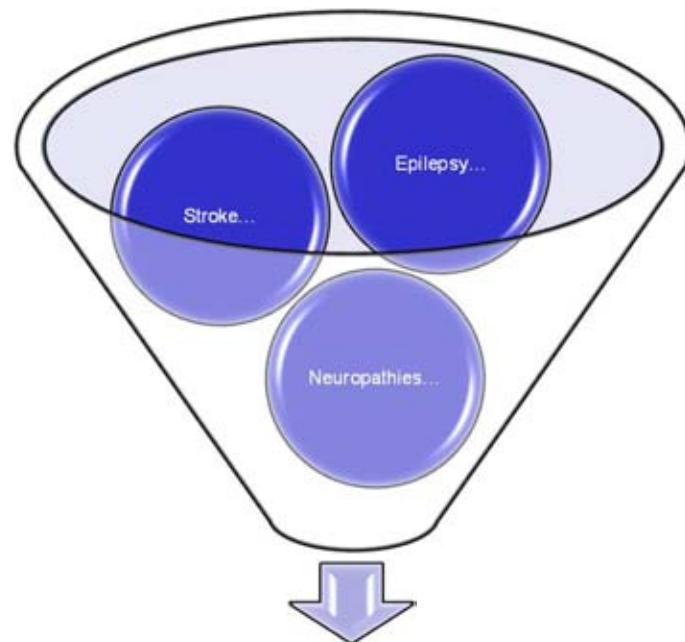
As usual, money is the point...

WFN could help in this matter

- Scholarships
- Funds to start the process of methodological units
- Seed money for starting research
- And then possibility to propose well developed ambitious protocols
 - Interregional
 - Comparative epidemiology
 - To raise and test new hypotheses

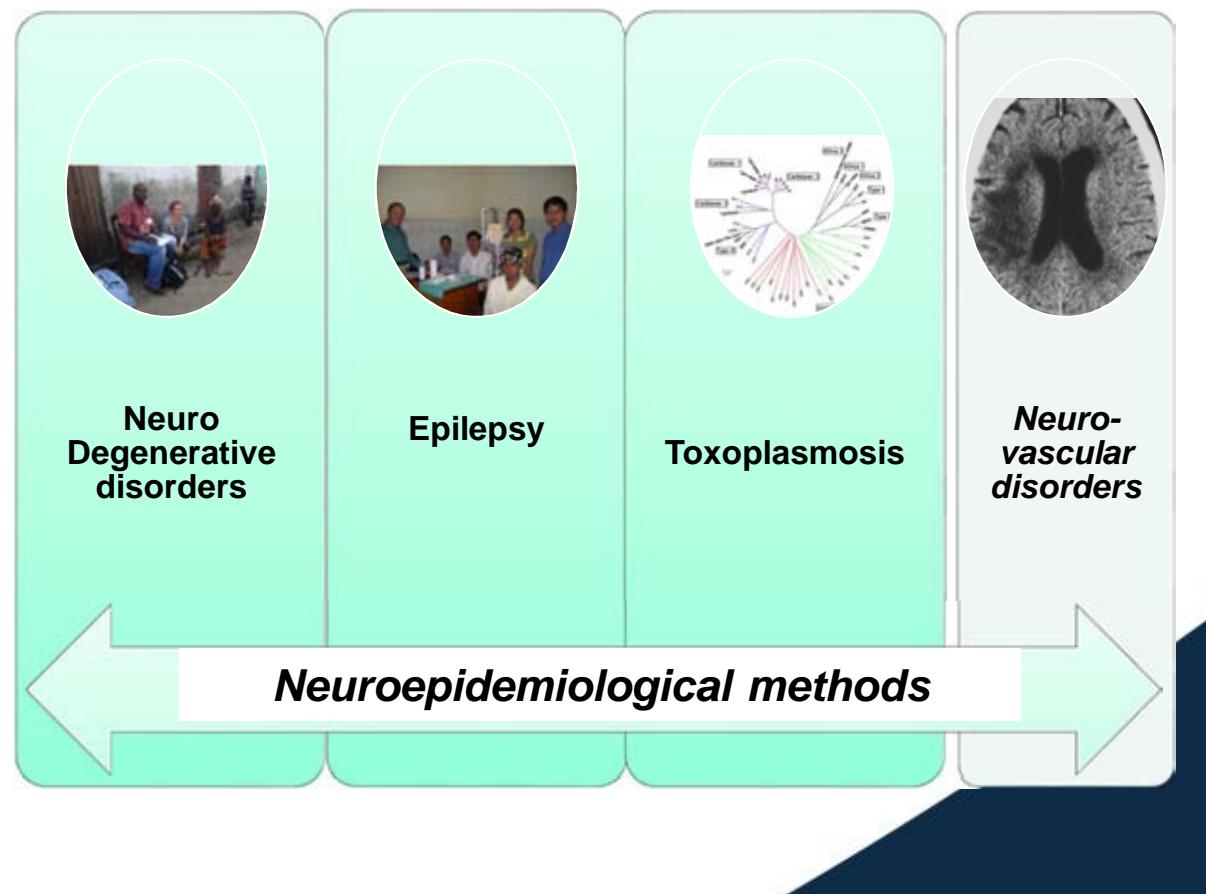
4. And then make many more studies...

Everybody could be involved!



Researches

Inserm U1094 Research axes 2012-2017



Concepts and methods in neuroepidemiology
research are worldwide the same

Neuroepidemiological research is feasible in Africa
and needs development



*Thank you for
your kind
attention*



Complementary slides

Box 2: Global Burden of Disease methodology

GBD uses thousands of data sources from around the world to estimate disease burden. As a first step, GBD researchers estimate child and adult mortality using data sources such as vital and sample registration systems, censuses, and household surveys. Years lost due to premature death from different causes are calculated using data from vital registration with medical certification of causes of death when available, and sources such as verbal autopsies in countries where medical certification of causes of death is lacking. Years lived with disability are estimated using sources such as cancer registries, data from outpatient and inpatient facilities, and direct measurements of hearing, vision, and lung function testing. Once they have estimated years lost due to premature death and years lived with disability, GBD researchers sum the two estimates to obtain disability-adjusted life years. Finally, researchers quantify the amount of premature death and disability attributable to different risk factors using data on exposure to, and the effects of, the different risk factors. For more information about the GBD methods, see the Annex of this report as well as the published papers.

Disability Adjusted Life Years (DALY)

The only differences in the rating of a death or disability should be due to age and sex, not to income, culture, location, social class. A common measurement unit for morbidity and mortality.

Everyone in the world has right to best life expectancy in world.

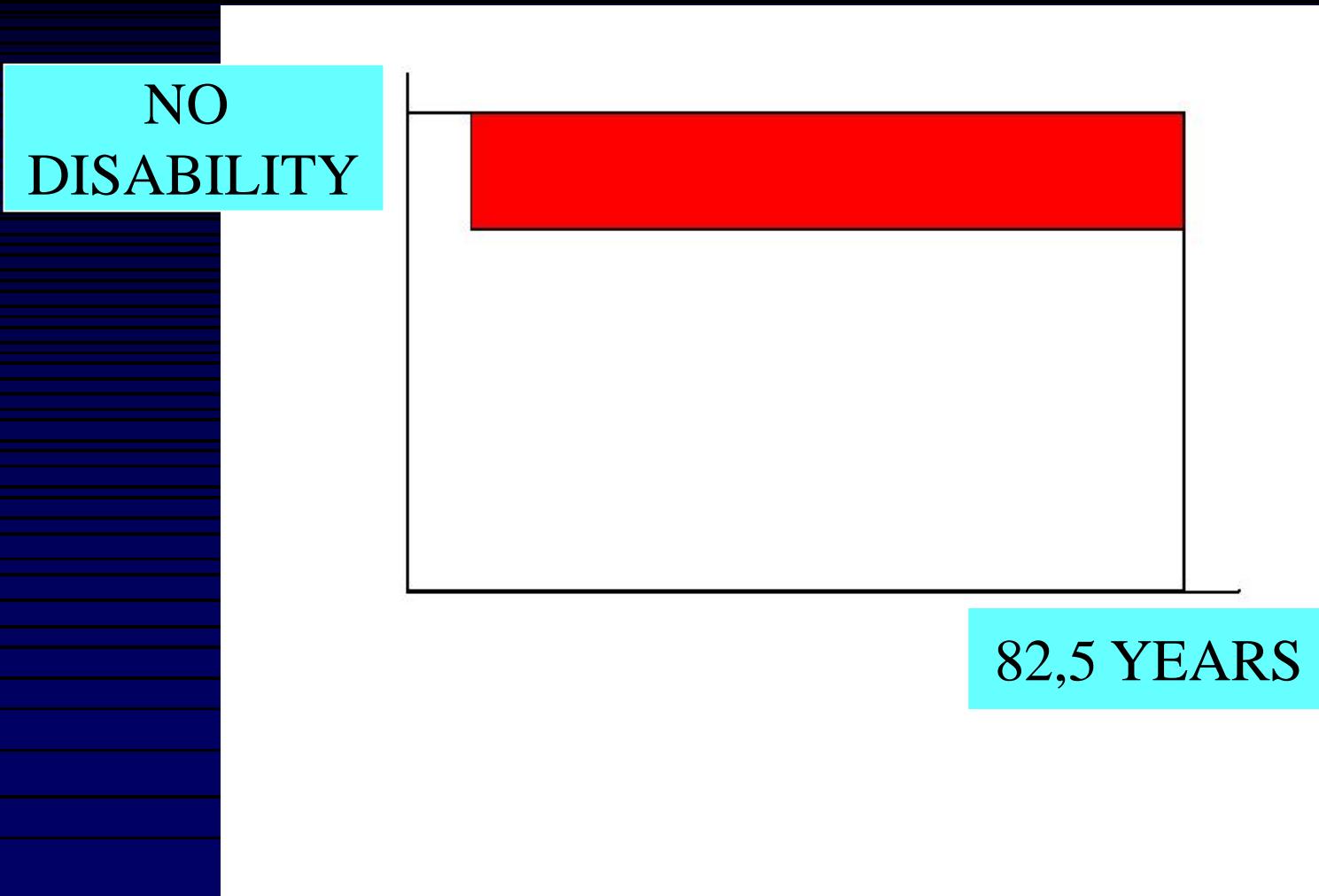
Facilitates comparisons of all types of health outcomes.

$$\text{DALY} = \text{YLL} + \text{YLD}$$

- Years of Lost Life (due to mortality)
- Years Lost to Disability (due to injury & illness)

DALYs due to living with disability

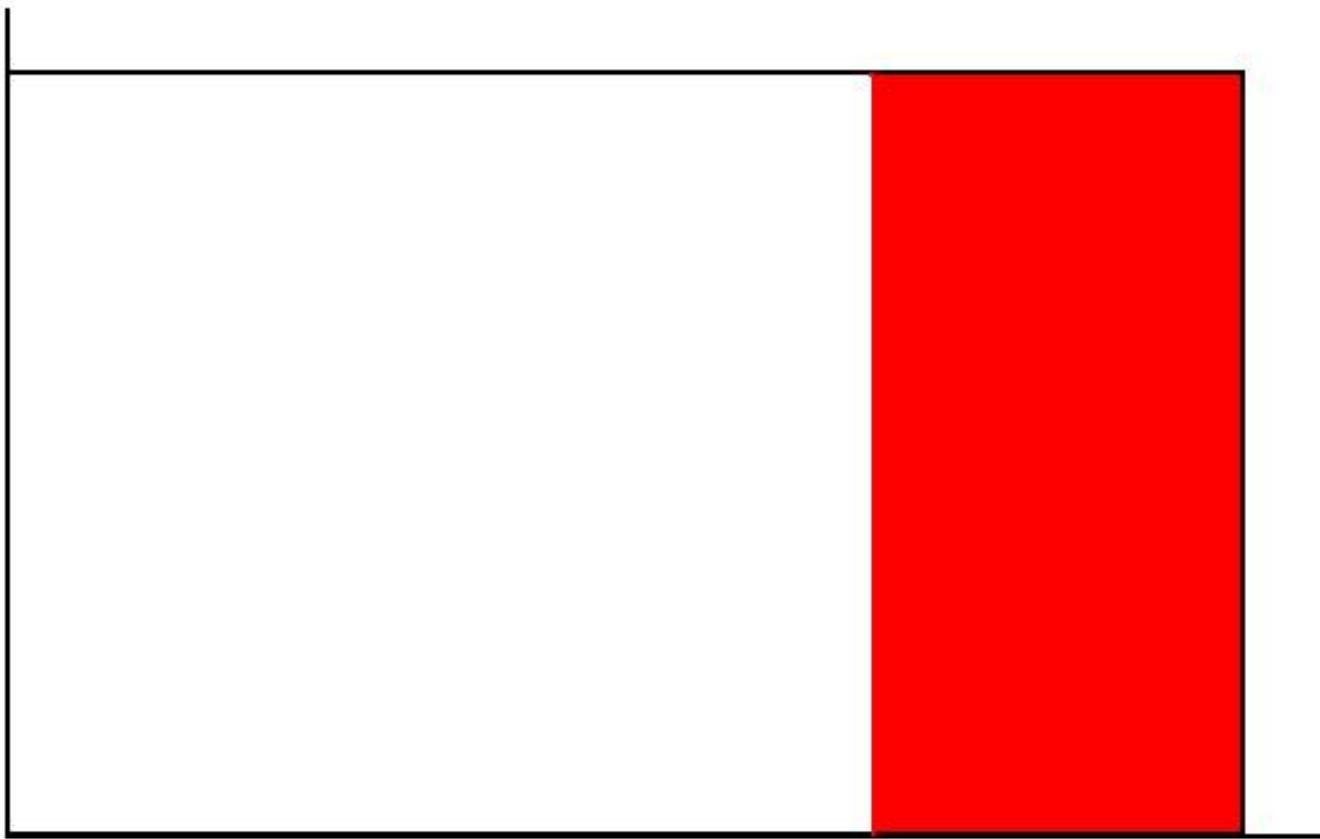
(Red area measures DALYs. Red + white is a “normal” life)



(Re)

NO
DISABILITY

No
disability



82,5 years

82,5 YEARS

NO
DISABILITY

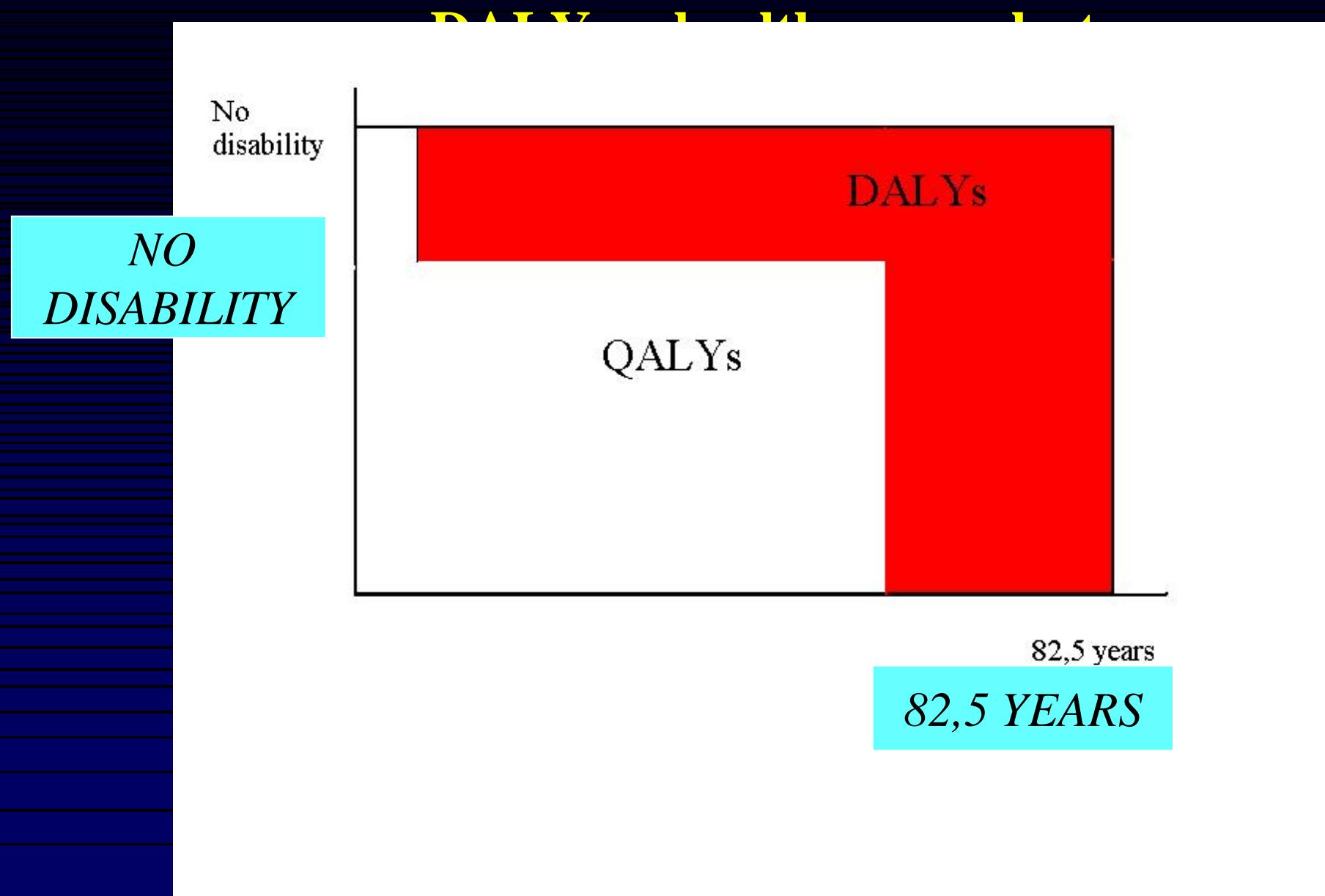
No
disability

DALYs

82,5 years

82,5 YEARS

Relation between QALYs and DALYs



DALY, GBD, 2010

- Progress on some communicable diseases but they stay on the top
- All of the neurological or mental health disorders increased between 1990 and 2010 (stroke, epilepsy, depression)

Figure 8: Shifts in leading causes of DALYs in sub-Saharan Africa, 1990-2010

