Epilepsy treatment in sub-Saharan Africa: closing the gap

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Summary

According to World Health Organization (WHO), the prevalence of epilepsy is highest in low- and lower middle-income countries, which include over eighty percent of the countries of sub-Saharan Africa, where the majority of people with epilepsy are not receiving appropriate care. In sub-Saharan Africa, shortages of trained health workers, limited diagnostic equipment, inadequate anti-epileptic drug supplies, cultural beliefs, and social stigma contribute to the large treatment gap for epilepsy. The number of people with epilepsy, particularly children, will continue to rise as a result of projected epidemiologic and demographic changes. This paper examines the state of epilepsy care and treatment in sub-Saharan Africa and discusses priorities and approaches to scale up access to medications and services for people with epilepsy.
Keywords: Africa, epilepsy, anti-epileptic.

Introduction

Neuropsychiatric disorders contribute 13.1% to the global burden of disease with epilepsy alone accounting for 0.5%[1,2]. Epilepsy is the most common neurological condition encountered by specialists in the WHO African region which is comprised of 47 countries representing sub-Saharan Africa[3]. These countries include some of the poorest in the world that are heavily dependent on development assistance for health, most of which is targeted to treat communicable diseases. According to the United Nations (UN) Population Division, the population of sub-Saharan Africa is estimated to double by 2050 to over 1.75 billion. As stated in the WHO report *Neurological Disorders: Public Health Challenges*[4]:

"A clear message emerges that unless immediate action is taken globally, the neurological burden is expected to become an even more serious and unmanageable problem in all countries."

This paper reviews the latest information on epilepsy prevalence and treatment in sub-Saharan Africa and analyzesthe costs and feasibility of interventions to reduce the treatment gap.

Literature search

Publications for this review were identified by a search of PubMed and CABI from 1985 through 2011 using the term "Africa" combined with each of the following keywords separately; "epilepsy", "seizure", "antiepileptic", "neurology", "health workforce", and "brain drain" . Additional references were sourced from the WHO-Afro Library and African Journals Online using the same keywords individually. The WHO publications were accessed from the website. Articles were selected if they included studies conducted in sub-Saharan Africa pertaining to the prevalence, diagnosis, care, or treatment of epilepsy. Since this is a health policy paper and not a meta-analysis or systematic review, no pre-specified selection criteria were used.

Prevalence of epilepsy

In 2005, the Global Campaign against Epilepsy coalition published the *Atlas; Epilepsy Care in the World 2005* which contains detailed information on epilepsy care in 160 countries representing 97.5% of the world's population[5]. This report gives an estimate of the prevalence of epilepsy in Africa of 11.29 per 1 000 population, resulting in 3, 367, 000 affected individuals. This is 26% higher than the worldwide mean prevalence of 8.93 per 1 000 population. However, they caution that "the data regarding the number of people with epilepsy were not collected using stringent research methods as for epidemiological studies". All information was obtained from one key individual working in the field of epilepsy for each country. A total of 38 African countries responded to the questionnaire accounting for 94.4% of the population in the region.

A number of studies of epilepsy prevalence in sub-Saharan Africa have been published, although different case definitions of epilepsy, survey methods,

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etiologies, age and sex distributions, and epilepsy-related mortality rates prevent direct comparison of unadjusted prevalence estimates. Dreux and Preut-Cabanac reviewed twenty-eight door-to-door surveys of epilepsy prevalence from fifteen countries in sub-Saharan Africa published between 1982 and 2004[6]. Only three studies were performed in urban populations. Smaller surveys (N<2 000) tended to report higher prevalence ratios. The largest community-based door-to-door survey (N=60 820) was conducted in a rural area of central Ethiopia and determined an epilepsy prevalence of 5.2 per 1 000[7]. A similar door-to-door survey was administered in a single large town in Nigeria where every eligible resident (N=18 954) was screened by survey teams consisting of teachers and non-doctor health workers[8]. Persons positive on the screening questionnaire and/or exam were further evaluated by neurologists and neurosurgeons. A prevalence rate for active epilepsy of 5.3 per 1000 residents was obtained with a slightly higher rate among females. Using a random cluster sample survey method including 18,000 persons, an epilepsy prevalence of 10.2 per 1000 was reported in the Ulanga district of Tanzania[9]. A door-to door survey in a rural catchment area of Zambia with a population of approximately 55 000 people found an unadjusted epilepsy prevalence of 14.5 per 1000[10].

More recent studies include a three-phase screening survey of 151 408 individuals conducted in 2003 in the rural Kilifi district in Kenya that determined an overall prevalence of active convulsive epilepsy of 2.9 per 1 000[11]. A 2005 national cross-sectional epilepsy survey in Rwanda (N=6 757) found an estimated prevalence of 7 per 1 000[12]. Due to limitations in the availability of electroencephalography and neuroimaging as well as incomplete medical histories, determining the etiology of epilepsy is usually difficult. Risk factors for epilepsy in sub-Saharan Africa include obstetric and perinatal problems, central nervous infections, and traumatic brain injury[13]. Many cases of epilepsy could be prevented through improvements in obstetric care, childhood immunizations, malaria prevention and treatment, and road traffic safety.

Assessing the treatment gap
Epilepsy represents approximately 0.5% of the total global burden of disease[1,2]. Of the more than 40 million individuals with epilepsy 80% live in developing countries where the vast majority does not receive appropriate treatment[5]. The epilepsy treatment gap (TG) is defined by the International League Against Epilepsy as follows[14]:
"The difference between the number of people with active epilepsy and the number whose seizures are being appropriately treated in a given population at a given point of time, expressed as percentage. This definition includes diagnostic and therapeutic deficits."

The reported size of the epilepsy TG in sub-Saharan Africa varies widely, ranging from 23% in Senegal to 100% in Uganda, Tanzania, Gambia, and Togo[15,16,17]. A 2003 study estimated a TG of 70.3% in the rural Kilifi district of Kenya based on undetectable amounts of anti-epileptic drugs in blood samples of people with active convulsive epilepsy[11]. In Togo, the TG in six primary care centers, determined by treatment interruption, ranged from 94% to 98% in 2008[18]. Larger national and regional surveys are needed to more accurately determine the size and variability of the epilepsy TG within and between countries.

There are a number of factors contributing to the TG for epilepsy in sub-Saharan Africa (Box 1).

Box 1: Leading causes of the epilepsy treatment gap

• Inadequate supplies and costs of anti-epileptic medications
• Lack of primary health workers trained to diagnose and treat epilepsy
• Limited access to health facilities particularly in rural areas
• Social stigma, misinformation, and traditional beliefs
• Limited opportunities for specialty training in neurology

One cause frequently mentioned in the literature is the influence of cultural beliefs on diagnosis and proper treatment[14]. Many people with epilepsy believe that their seizures are due to supernatural forces and consequently spend considerable personal time and financial resources seeking remedies from traditional healers. Even in developed countries, people with epilepsy often feel stigmatized and may avoid seeking treatment[19]. Specialist care for epilepsy is usually unavailable at the community level and patients frequently need to travel long distances for proper diagnosis and treatment. Difficulty in traveling to obtain care was the main reason given for default from follow-up at a rural epilepsy clinic in Ethiopia[20].

The mean duration for round-trip travel to the health center was greater than 10 hours.

In most countries, phenobarbital is the only antiepileptic medication in widespread use. Other standard drugs for epilepsy, including phenytoin, carbamazepine, and valproic acid, are commonly available but are significantly more costly[21]. Phenobarbital is rarely prescribed in the United States and Europe because of its relatively greater side effects, but it remains an effective and inexpensive drug that can be taken once daily. Unfortunately, consistent access to anti-epileptic drugs is cited by the ILAE as "both a cause of the treatment gap and the single most important obstacle to bridging the gap"[14]. In a recent analysis of drug availability surveys conducted in 40 developing countries including 12 countries of sub-Saharan Africa, phenobarbital and/or phenytoin was available in only 40.3% and 29.4% of facilities in the private and public sectors respectively[22]. Despite its low cost, some patients in the poorest countries may still find the drug unaffordable. Compliance is a frequent problem since patients do not always appreciate the need to take daily medication for an intermittent condition. Medication toxicity and drug-drug interactions are additional concerns. Unreliable supplies of medications, especially at rural clinics and dispensaries, make it difficult for many patients to maintain therapeutic blood levels. Finally, substandard and counterfeit medications are growing concerns affecting mostly developing countries[23,24].

Inadequate skilled manpower was the largest contributor to the epilepsy TG in developing countries according to the review by Mbuba et al[17]. The median number of neurologists in sub-Saharan Africa is estimated at 0.3 per 1 million population, with 11 countries having none[25]. Only 11 countries have more than 10 neurologists per country. These statistics are in sharp contrast to Europe where there are 48.4 neurologists per 1 million population[3]. Post-graduate neurology training programs are only available in a few countries of sub-Saharan Africa[3]. The deficiency of neurologists translates into sparse neurological training of primary care physicians, clinical officers, nurses, and community health workers. Finally, the supply of diagnostic equipment to aid in the management of epilepsy (EEG machines, CT and MRI scanners) is extremely limited in many parts of Africa[26].

Closing the Gap – Interventions

Based on the discussion above, a multitude of interventions are necessary to reduce the epilepsy treatment gap in sub-Saharan Africa. At the international level, increased advocacy for epilepsy is necessary to raise awareness of this condition as a major non-communicable disease. Epilepsy is frequently viewed, incorrectly, as a non-fatal and non-disabling condition. People with epilepsy have a mortality rate 2-3 times higher than the general population[27]. Causes of death include status epilepticus (prolonged uncontrolled convulsions), sudden unexplained death in epilepsy (SUDEP), and suicide. Educational achievement, employment rates, and quality of life are all substantially lower for people with epilepsy[28]. Furthermore, disability rates and associated costs are higher. The Global Campaign Against Epilepsy was started in 1997 to bring epilepsy "out of the shadows"[29]. More epidemiologic research is needed to document the social and economic impact of epilepsy in sub-Saharan Africa for policy makers and funding agencies[30].

Increasing the supply of health workers capable of diagnosing and treating epilepsy is a critical need. The small numbers of, or lack of, physicians trained in neurology in many countries represents an obvious deficiency that can only be remedied by additional post-graduate training programs, partnership with neurology training programs in developed countries, and incentives to retain neurologists and reduce the 'brain drain'. The majority of people with epilepsy in sub-Saharan Africa will need to be treated by primary healthcare providers at the community level. Therefore, neurologists will need to engage in organized educational programs to train primary care physicians, clinical officers, nurses, and community health workers, so they can carry out the basic services required to manage epilepsy. This task-shifting can only be accomplished if government health ministers, regional and national neurological associations, and funding agencies work synergistically to disseminate neurological knowledge to lower cadres of health workers.

Primary healthcare providers should be trained to administer validated screening surveys and perform simple neurological exams in their communities to identify residents with possible epilepsy. A neurologist (or physician specializing in epilepsy) can review all positive screening results to confirm a diagnosis of epilepsy. The neurologist

may be located at a higher level district or regional hospital or may visit the rural clinic on a regular schedule. The neurologist can help facilitate any required diagnostic testing (EEG, CT, MRI, lab tests) and recommend appropriate anti-epileptic medication. The primary provider is then responsible for managing the patient's condition including: 1) tracking seizure frequency (using patient-maintained seizure calendar), 2) monitoring medication compliance and side effects, 3) ordering laboratory tests and drug levels, and 4) providing education and social support. A community-based intervention trial using a similar protocol was successfully implemented in rural China[31].

Reliable procurement and distribution of anti-epileptic medications at low cost are critical. Lack of drug supply is reported as a major problem in three-quarters of low-income countries[5]. A 2001 cohort study in a rural area of Cameroon found that only 16 of 91 patients were taking antiepileptic drugs every day[32]. In a study of 352 people with epilepsy in an agricultural region of Burundi[33], only 18 of the patients were taking anti-epileptic medications (all on phenobarbital). Phenobarbital is the recommended first-line medication by the WHO and is the cheapest with a median cost in international dollars of only $0.12 per daily defined dose (100 mg) (WHO 2005). An international dollar is a hypothetical currency that has the purchasing power of one US dollar in the United States. The second most prescribed drug, phenytoin, is considerably more expensive at $0.50 per daily defined dose (300 mg). In Uganda and Kenya, generic phenobarbital, phenytoin, and carbamazepine are available at higher level government health facilities (author, personal observations 2010-11). Some private retail pharmacies in both countries carry sodium valproate, gabapentin, and lamotrigine, although the cost of these antiepileptic drugs is beyond the financial reach of most patients. Although phenobarbital has a number of significant drawbacks as a first-line medication for epilepsy[34], it is probably the only drug with reasonable potential for widespread scale up and acceptance since out-of-pocket expenses are the main source of healthcare financing in most of sub-Saharan Africa[5].

Finally, closing the gap in epilepsy care will require the dissemination of culturally appropriate information about seizures and the importance of proper medical treatment. In many communities, people with epilepsy are not seeking appropriate treatment because of social isolation, superstition, and/or reliance on traditional healers. Increasing patient knowledge through community-based education programs can enhance medication compliance, improve seizure outcomes, and reduce stigma[35].

Closing the Gap – Financing

The cost of reducing the treatment gap for epilepsy in low-income countries has received little attention. Any economic analysis must first determine which services and programs are essential to provide basic epilepsy care in a particular country or region. In addition, the positive offsets of reduced healthcare service needs, lower mortality, and improved work productivity need to be considered. In the case of sub-Saharan Africa, the two most important interventions are increasing the supply of phenobarbital to all levels of healthcare delivery and increasing the number of health workers trained to diagnose and treat epilepsy.

Assuming that 80% of the 3 367 000 PWE living in the WHO African region[5] are not receiving anti-epileptic medication and the median cost of the least expensive drug phenobarbital is $0.12 per daily defined dose (100 mg)[5], the minimum annual cost to close the medication gap would be $117 979 680. Including phenytoin to treat 25% of patients at a cost of $0.50 per daily defined dose (300 mg) would almost double this figure. According to estimates based on two WHO African sub-regions, increasing coverage of first-line antiepileptic drugs (phenobarbital, phenytoin, carbamazepine, and valproic acid) to 50% of epilepsy patients would reduce disability-adjusted life years by 32-40% at an annual patient cost per year of 71 to 161 international dollars[21]. These estimates combine costs for drugs, laboratory tests, and primary/secondary health care. Providing even more expensive newer generation antiepileptic medications is not likely to be sustainable for most low-income countries.

Training more neurologists locally and retaining them would require a significant financial investment. The total cost of educating a single medical doctor in Kenya, from primary school through medical school, has been estimated at $65 997 [36]. Given the fact that there are only 0.3 neurologists per 1 million population in Africa, the cost to increase the number of neurologists to the WHO recommended minimum of 1 per 100, 000 population[25] would be substantial. In 2009, there were only 267 neurologists in all of sub-Saharan Africa[37]. Post-graduate training in neurology should be concentrated and supported

at established medical schools in selected countries. Some neurologists would need to be sponsored for epilepsy fellowship training in Europe or the United States. Most importantly, working conditions, salaries, and benefits would have to be attractive enough to prevent newly trained neurologists from emigrating to wealthier countries seeking highly skilled professionals[38].

Concurrent with the training of more neurologists, educational activities will need to be developed and supported to teach primary healthcare workers basic skills in diagnosing and managing epilepsy. These programs will require partnerships between government agencies, non-governmental organizations, and professional societies. The World Federation of Neurology and the WHO have already made commitments to support educational initiatives for physicians and non-physicians[39]. Much of this training will depend on volunteerism by neurologists from developed countries. Distribution of evidence-based and easy-to-follow manuals to evaluate and treat seizure disorders, such as the WHO mhGAP intervention guide[40], will help facilitate the process of task-shifting to non-specialist health providers.

Recommendations
The future of epilepsy treatment in sub-Saharan Africa will remain challenging given the many barriers discussed in this review. Recommendations to guide policy development and program planning are listed in box 2. Continued advocacy for people with epilepsy will require more epidemiologic research to document the true burden of disease and magnitude of the treatment gap in different countries. In the short term, improving the availability of phenobarbital and other generic first-line antiepileptic drugs should be given the highest priority. The more difficult challenge will be to increase the number of skilled healthcare workers capable of diagnosing and treating epilepsy. International neurological organizations, including the International League Against Epilepsy, the International Brain Research Organization, the World Federation of Neurology, and the American Academy of Neurology, should increase their efforts to develop and support epilepsy training curricula and programs.

Box 2: Recommendations for improving epilepsy care and treatment

- Include all oral antiepileptic medications on the WHO Model List of Essential Medicines in approved national drug formularies (phenobarbital, phenytoin, carbamazepine, and valproic acid/sodium valproate)
- Create regional purchasing pools for antiepileptic drug procurement and improve supply chain management
- Develop contextually appropriate programs and provide community education about the causes and treatment of epilepsy
- Partner with tribal, religious, and community leaders to disseminate information and combat stigma and discrimination
- Train nurses and clinical officers to manage patients with epilepsy and integrate services into existing local primary care programs, particularly in rural areas
- Organize and support regional, national, and district level surveys to assess the epilepsy burden, barriers to care, and resource needs
- Foster and facilitate regional and international collaborations to create epilepsy training opportunities for both neurologists and primary healthcare providers

Conclusion
In the last decade, the disproportionate majority of global health funding has been allocated to vertical programs targeting HIV/AIDS, malaria, and tuberculosis[41]. The renewed calls for action to raise the priority of chronic non-communicable diseases in global health planning and research are encouraging[42]. Funding commitments from domestic governments, international donors, non-governmental organizations, industry, and private

philanthropists will be critical to scaling up access to anti-epileptic medications and building capacity in human resources for epilepsy care in sub-Saharan Africa.

A Global Fund for Epilepsy should be established to accelerate donor support and coordinate program development and implementation, both in sub-Saharan Africa and in other resource-limited regions of the world.

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