From DEPARTMENT OF CLINICAL NEUROSCIENCE
Karolinska Institutet, Stockholm, Sweden

EPIDEMIOLOGY AND CARE OF EPILEPSY IN VIETNAM

Nguyen Anh Tuan

Karolinska Institutet

Stockholm 2010

From DEPARTMENT OF CLINICAL NEUROSCIENCE
Karolinska Institutet, Stockholm, Sweden

EPIDEMIOLOGY AND CARE OF EPILEPSY IN VIETNAM

Nguyen Anh Tuan

Karolinska Institutet

Stockholm 2010

Published by Karolinska Institutet. Printed by Larserics Digital Print AB

ISBN 978-91-7409-912-6

ABSTRACT

Epilepsy is often considered the most common serious chronic neurological disorder estimated to affect 50 million people globally. Although the majority of these live in developing countries, data on the epidemiology of epilepsy from such countries are scarce. This is true also for Vietnam. The overall objective of this project, Epidemiology and Care of Epilepsy in Ba Vi (EPIBAVI), was therefore to provide essential epidemiological data on epilepsy in Vietnam as a basis for an improved management of people with epilepsy in the country.

Four studies were carried out in Ba Vi, a representative rural district in the Ha Tay province, utilizing the epidemiological field laboratory FilaBavi. We first assessed public knowledge, attitudes and practice toward epilepsy by application of a WHO questionnaire to 2,005 persons from Ba Vi. Knowledge of epilepsy among the interviewed was found to be limited compared to in some Western countries and attitudes clearly more negative. As examples, 36% would object to their children playing with someone with seizures and 82% to their children marrying someone with epilepsy.

Utilizing a validated screening questionnaire, approximately 50,000 people in the region were questioned in their homes by trained interviewers to identify potential cases of epilepsy. All who were screened positive in these surveys were subsequently examined by a neurologist to confirm or refute the epilepsy diagnosis. In total 40 incident cases (two surveys combined) and 206 prevalent cases of active epilepsy were thus identified. Age-adjusted incidence was 44.8/100,000 (95%CI 30.6-59.0), higher in those under 16 years, among people with lower education, and with lower income. Age-adjusted prevalence was 4.4 per 1,000 (95%CI 3.8-5.0), higher among males, 5.1(4.1-5.9), than females, 3.8(3.0-4.6), and among those with lower compared with higher education and among single compared with those married. CT-scan of the brain revealed the etiology of epilepsy in a very small proportion of the incident cases.

Cases with active epilepsy were interviewed about their treatment, and 84.7% (95%CI: 79.5% - 89.8%) were found not to be on adequate drug treatment. The most common reasons for not taking antiepileptic drugs expressed by the patients was the perception that their seizures were too few to justify the trouble and costs associated with treatment.

In conclusion, the incidence and prevalence of active epilepsy in Vietnam and the association with socio-economic conditions is similar to the patterns reported from Europe and North America. Only 15% of people with active epilepsy in the present study were on adequate drug treatment despite a national programme providing some drugs free of charge. Patient as well as public education about epilepsy and its treatment is needed.

Keywords: Knowledge, attitudes, practice, prevalence, incidence, treatment gap, epilepsy, seizures, Vietnam

LIST OF PUBLICATIONS

I Tuan NA, Cuong LQ, Allebeck P, Chuc NT, Tomson T. Knowledge Attitudes and Practice toward Epilepsy among Adults in Ba Vi, Vietnam: First Report from the Population-Based EPIBAVI Study. Epilepsia. 2007; 48(10): 1914-9

II Tuan NA, Cuong LQ, Allebeck P, Chuc NT, Persson HE, Tomson T. The prevalence of epilepsy in a rural district of Vietnam: A population-based study from the EPIBAVI project. Epilepsia. 2008; 49(9): 1634-7

III Tuan NA, Cuong LQ, Allebeck P, Chuc NT, Tomson T. The Treatment Gap of epilepsy in a rural district of Vietnam: A study from the EPIBAVI project. Epilepsia. 2009; 50(10): 2320-3

IV Tuan NA, Cuong LQ, Allebeck P, Chuc NT, Persson HE, Tomson T. The Incidence of epilepsy in a rural district of Vietnam: A population-based study from the EPIBAVI project. (Submitted)

CONTENTS

LIST OF ABBREVIATIONS

AED	Antiepileptic drug
CT-Scan	Computed tomography scan
EEG	Electroencephalogram
EPIBAVI	Epidemiology and Care of Epilepsy in Ba Vi
Filabavi	Epidemiological Field Laboratory in Ba Vi district, Hanoi, Vietnam
ILAE	International League Against Epilepsy
KAP	Knowledge, attitudes and practice
SUDEP	Sudden unexpected/unexplained death in epilepsy
WHO	World Health Organization

1 BACKGROUND

1.1 EPILEPSY AND SEIZURES

1.1.1 Some historical aspects

With its dramatic manifestations, epilepsy has been recognized since the earliest medical as well as other writings, and few medical conditions have generated so much controversy as epilepsy. The earliest known text on epilepsy is contained in tablets in Babylonian cuneiform writing dating from the 7th century BC (1).

The word "Epilepsy" is derived from the Greek word "epilepsia," which means "to take hold of" or "to seize." This meaning is very close to what Babylonians believed to be the cause of epilepsy (2). Babylonians used the verb "sibtu" to denote epilepsy, which means "being seized." Epileptic seizures was then believed to begin with possession by a demon and ended when the demon departed the body.

Hippocrates wrote the first known book on epilepsy, refuting the common idea that epilepsy is a curse or a prophetic power, He concluded that "It is thus with regard to the disease called Sacred: it appears to me to be nowise more divine nor more sacred than other diseases, but has a natural cause like other affections. . ."

Nevertheless, the idea that epilepsy is an expression of supernatural powers, e.g. obsession of evil spirits or demons invading a person's body, has until recently prevailed through history. Numerous examples can be found in religious as well as secular texts. In the Gospel According to Mark (9:14-29), Jesus Christ casts out a devil from a young man with epilepsy: "Teacher, I brought you my son, who is possessed by a spirit that has robbed him of speech. Whenever it seizes him, it throws him to the ground. He foams at the mouth, gnashes his teeth, and becomes rigid. I asked your disciples to drive the spirit out, but they could not."

The work of the 19th century English neurologist John Hughlings Jackson marks the beginning of the modern medical era of epilepsy. Jackson defines a seizure as "an occasional, an excessive, and a disorderly discharge of nerve tissue on muscles." He recognizes the association between the clinical seizure manifestations and their origin in the brain (3).

Another major contribution to our understanding of the nature of epilepsy came with the discovery of the German psychiatrist Hans Berger, who in 1929 showed that it was possible to record from the surface of the skull electric currents generated in the brain (4). Berger named this form of recording as the electroencephalogram (EEG), and it was subsequently demonstrated that there were changes in the EEG during and between seizures in people with epilepsy (5).

Nevertheless, attitudes of past societies toward epilepsy have left a legacy of stigma and damaging misconceptions which still persist today, as people with epilepsy continue to face fear, prejudice and discrimination in their everyday lives.

1.1.2 Epilepsy in Vietnamese and Asian cultures

"Religion and literature on epilepsy" were explored in the 2004 Asian Oceanian Epilepsy Congress (6). In traditional Chinese medicine, epilepsy is not thought to be brought about by any supernatural agents. The Chinese translation of epilepsy is "Dian", meaning falling sickness and epileptic attack is "Xian", meaning convulsion.

Chinese medicine evolved with little outside interference and has maintained its coherence throughout its development (7). Ancient Chinese medical texts provided many accounts of Dian and Xian. However, the word Dian could refer to either psychosis without excitation or epilepsy (8). This makes it hard to know whether ancient documentation of Dian actually referred to epilepsy or psychosis. In fact, epilepsy was at one time placed among Dian (psychoses without excitation), "Kuang" (psychoses with excitation), and Xian (convulsion) as one class of psychiatric disorders within the context of traditional Chinese medicine. The clinical presentation of people with Xian was described as someone falling to the ground suddenly with eyes closed, seemingly asleep (9).

In the Shu-Wen volume of Huang Di Nei Jing, meaning Internal Medicine of the Yellow Emperor, believed to be written by a group of Chinese physicians about 779 to 221 B.C. (10), an explanation of the etiology of epilepsy could be found. The cause of Dian in children should be traced to their pre-natal period, when their mothers suffered from an emotional shock, a bad scare, causing the obstruction of vital air, causing the illness (7). Another account about Dian in Huang Di Nei Jing made a clear reference to the connection between Xian and dysfunction of the head and the hepatic system. In another account, Dian was connected with excessive negative force (Yin) (11).

More precise descriptions of epilepsy were found in Qi Xiao Liang Fang and Zheng Zhi Zhun Sheng; both were written in the Ming Dynasty by Wang Ken Tang and Fang Xian respectively (10). Wang reported epileptic attacks usually consisted of convulsions with loss of consciousness, frothing, and vocalization.

In other Asian countries and in Vietnam, the translation of the term epilepsy has negative meaning. The term epilepsy in Vietnamese is "dong kinh" while "dong" means "moving or convulsion" and kinh means "terrible".

As in China, lay informants in Vietnam were clear that as a disease ''inside the body,'' epilepsy was not ''transmittable'' to others; again, however, opinions were divided as to whether epilepsy could be inherited. The question as to the heritability of epilepsy was linked to a lay theory that seizures often resulted from ''weak nerves'' and that such weakness was itself hereditary. Following from this, factors such as stressful life events and heavy work or overwork were seen as exaggerating any such weakness and so acting as triggers for seizures. Other common attributions were that epilepsy was linked to fever (a common sense interpretation of the onset of seizures in an area where malaria, dengue fever, and Japanese encephalitis are all endemic) and to exposure to the chemical Agent Orange. Epilepsy was only rarely attributed to sins committed in a previous incarnation, fate, or magical causes. In keeping with traditional medicine theory focusing on phong (wind), seizures were also commonly

thought to be triggered by extremes of weather, such as strong winds, or seasonal weather changes (12).

Up to now, Vietnamese health care workers recognized epilepsy as a condition with multiple causes, including accidents and head injury; birth trauma; infections such as encephalitis, meningitis, tetanus, and tuberculosis and accompanying high fever; hypertension; and blood circulation problems. However, they also pointed to the delineation in traditional medicine of three categories of disease causation: internal psychological causes such as sadness, depression, and anger; external environmental causes, in particular climate and weather changes; and other causes, including falls and food poisoning. Health care workers were all confident that epilepsy was not contagious but in some instances had a genetic basis, specifically with mother-to-child transmission (12).

1.1.3 Current definitions and classification of seizures and epilepsy

Seizures are the fundamental elements of epilepsy and are symptoms of abnormal brain function. An epileptic seizure is defined as the transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain (13). As realized already by Hughlings Jackson in the 19th century, the clinical manifestations of the seizures depend on the functional region of the brain that is involved in the abnormal neuronal activity. This has also been the basis for the classification of epileptic seizures. The currently used classification of seizures was published in 1981 by the International League Against Epilepsy (ILAE) and is based on the clinical manifestations of the seizure and EEG findings (14). The primary dichotomy in the seizure classification depends on whether the seizure originates in a restricted part of the brain (partial or focal seizures) or involves both hemispheres from onset (generalized seizures). Partial seizures are subdivided into simple (with maintained consciousness), complex (consciousness impaired) or partial secondarily generalized (seizure activity spreads to involve both hemispheres). There are also different types of generalized seizures, e.g. absences, myoclonic seizures, and generalized tonic-clonic seizures. A seizure with unconsciousness and major convulsions could thus be either partial secondarily generalized or primary generalized depending on the mode of onset. This is sometimes difficult to ascertain. The international classification of seizures includes a third category, unclassified seizures, for such cases were sufficient information for categorisation is lacking.

The definition and classification of seizures is not the same as that of epilepsy. While the seizure is the fundamental element and symptom and sign of epilepsy, the latter is defined as a chronic condition characterized by recurrent unprovoked epileptic seizures (13). The current classification of the epilepsies and epileptic syndromes of the ILAE dates back to 1989 (15) and stratifies epilepsies into four major categories based on the presumed site of origin of the seizures (localization-related or generalized) and the etiology of the seizures (idiopathic or cryptogenic or symptomatic). The current classification is under revision as it is considered to be based on concepts that, for most part, predate modern neuroimaging, genomic technologies and concepts in molecular biology (16). Nevertheless the quoted classifications of seizures and epilepsies are still in use and are valuable tools for diagnosing people with seizure disorders, for decisions on etiological work up, for selection of appropriate therapy and for the prediction of prognosis.

1.1.4 Etiology of epilepsy

Epilepsy is often, but not always, the result of an underlying brain disease. Any type of brain disease or injury can cause epilepsy, but not all people with the same brain disease will have epilepsy. This implies an individual susceptibility to develop seizures and epilepsy.

The 1993 ILAE recommendations for epidemiologic studies (17) suggested dividing symptomatic epilepsy into ‘‘remote’’ and ‘‘progressive’’, where remote symptomatic epilepsies encompass cases developing following insults resulting in static lesions (such as those attributable to conditions such as stroke or CNS infections), and progressive symptomatic epilepsy encompass epilepsies associated with non-static conditions (such as brain tumours or degenerative disease).

In studies including all ages, an identified cause is present in 14—39% of cases, while the majority has no obvious identifiable cause (18).

It is likely that there are some differences in etiologies of epilepsy in developed and developing countries although solid evidence from well designed studies are lacking. It nevertheless seems that cerebrovascular diseases, traumatic brain injuries, tumours and dementia dominate in developed countries while CNS infections are more frequent in developing countries. In Sub-Saharan Africa and Latin American, CNS infections including malaria, tuberculosis, schistosomiasis, cysticercosis, and AIDS might contribute to the high incidence and prevalence of epilepsy in these regions (19).

1.2 EPIDEMIOLOGY OF EPILEPSY

1.2.1 Incidence and prevalence in general

Epilepsy is often called the most common serious chronic neurological disorder, estimated to affect approximately 50 million people world wide (18). Epilepsy has no ethnic, geographical, or socio-economic barriers, and affects all ages and both sexes. However, prevalence rates vary widely from study to study. It is not clear to what extent these differences are real or spurious due to differences in definition and methodology between studies. The ILAE has issued guidelines to standardize epidemiological research on epilepsy and thus facilitate comparison between studies (17, 20), but these have often not been adhered to.

Accurate data on prevalence and incidence are important to determine those who are at risk of epilepsy, understand the etiology and thus possible preventive measures, and not least in order to provide adequate epilepsy management services. Although it has been estimated that approximately 80% of people with epilepsy live in developing countries (21), the vast majority of studies on the epidemiology of seizures and epilepsy have been carried out in the western industrialized world.

Incidence rates of epilepsy in Europe and North America have generally ranged from 30 to 50/100,000 person-years (18). There appears to be some geographical variation in the incidence of epilepsy, with a higher incidence in rural South America than in developed countries, 113 to 190/100,000 person-years (22-25). No large scale population-based incidence studies have yet been carried out in Africa or Asia. A consistent pattern with higher incidence of epilepsy in

early life and among the elderly has also been shown (26-29). The incidence also appears to be slightly higher among males (27, 29, 30).

Prevalence rates for active epilepsy have generally ranged from 4 to 15/1,000 (31). The highest rates have been reported from developing countries in South America and Africa (23, 28), whereas the prevalence of active epilepsy has often been reported to be in the lower range in countries from Asia (26). Differences in definitions and methods for case ascertainment could account for some of this variation. However, true differences between populations in the prevalence of epilepsy are likely to exist due e.g. to differences in etiological factors. It has frequently been claimed that the incidence of epilepsy is considerably higher in developing countries whereas the difference in prevalence rates is less pronounced (32). It has been speculated that this discrepancy could be explained by a higher mortality among people with epilepsy in developing countries that are less likely to get adequate treatment (33). Clearly, epidemiological data cannot readily be extrapolated from one study to other regions and population-based studies are thus needed from different parts of the world.

The ILAE, the International Bureau for Epilepsy and the World Health Organization (WHO) have joined forces in a Global Campaign Against Epilepsy aiming at raising awareness of epilepsy and at facilitating appropriate treatment for those untreated (34). As part of this campaign epidemiological demonstration projects have recently been implemented in some developing countries in order to estimate the prevalence of untreated epilepsy (35).

1.2.2 Incidence and prevalence of epilepsy in Asia and Vietnam

Over half of the 50 million people with epilepsy worldwide are estimated to live in Asia. Asia is a heterogeneous and resource-constrained continent. A recent systematic review reported on the epidemiology of epilepsy in Asia (26). Prevalence rates ranged from 1.5 to 14 per 1,000 people. The median lifetime prevalence rate was estimated to be 6/1,000 people.

Very few studies have been published on the incidence of epilepsy in Asian countries (36, 37). In these, the incidence has been lower than in Latin America and Africa, 29-35/100,000 in China (36, 38) and 49/100,000 in India (37). Age-adjusted incidence was 35/100,00 in the only study where such adjustment was possible (18, 37). There are no similar studies from Vietnam that have been published in full. One door-to-door survey, so far published only in abstract, reported a considerably higher prevalence of 10.7 per 1,000 (39) but this was from a region with a high incidence of neurocysticercosis.

1.3 CONSEQUENCES OF SEIZURES AND EPILEPSY

Epilepsy can have serious consequences. In addition to restrictions in daily life imposed by uncontrolled seizures, such as for driving license and for employability in some professions, seizures with sudden falls and unconsciousness can cause physical injuries (40).

There is also an increased mortality rate among patients with epilepsy, 2-3 times that of the general population (41). This has a peak in the first year after diagnosis as a result of those causes of epilepsy that have high case fatality, such as brain tumours, subarachnoid haemorrhage and stroke. However, the mortality rate remains elevated, particularly among

young adults with severe active epilepsy. Epilepsy-related deaths could be in status epilepticus or sudden unexpected death (SUDEP). The annual incidence of SUDEP varies from 1/10,000 person years among new onset epilepsy patients to up to 1/100 person years in patients with chronic refractory epilepsy (42). The risk appears to be closely associated with the frequency of seizures. A recent population-based study of epilepsy patients in China suggests an even higher excess mortality compared to developed countries (43).

Adding to the medical and physical consequences, many of the old superstitions still stand against those with epilepsy, especially in developing countries, making it particularly difficult for them to live normal lives.

1.4 PROGNOSIS OF EPILEPSY

In general, a third to two-thirds of patients will have recurrent seizures within 5 years of the first unprovoked seizure. Similar recurrence rates are seen in Asia. A study in Thai children showed a cumulative risk of recurrence of 25% at 14 days, 50% at 4 months, 51% at 6 months, and 66% at 12 months (44). The risk of further seizures after a second seizure is even higher and treatment with antiepileptic drugs (AEDs) is generally considered indicated in this situation (45, 46). Treatment with AEDs is symptomatic and there is now evidence that they affect the natural course of epilepsy. However, approximately 50% will respond with seizure control to the first prescribed AED. Up to 70% to 80% will enter remission after trying alternative or additional AEDs. Experiences from a developing countries such as India and China are encouraging, suggesting a high response rate to phenobarbital even among patients with prior long-standing epilepsy (33, 47, 48).

As 70–80% of patients on AEDs become seizure free, it is common clinical practice to consider withdrawal once a patient has been in remission for a 'reasonable' length of time. The largest randomized study of AED withdrawal in seizure free patients found a risk of relapse of 41% within 2 years of drug withdrawal, compared with a rate of 22% among the group randomized to continuing with medication (49). Hence, although there is a significant risk of relapse also after several years of seizure freedom, this and other observations (50) clearly demonstrate that many patients with epilepsy will recover after some years of treatment.

1.5 TREATMENT OF EPILEPSY

1.5.1 General aspects of treatment

The treatment of epilepsy aims at achieving the best possible quality of life for the patient according to their individual conditions. In most cases this means aiming at complete control of seizures. Treatment can include a range of measures from avoidance of seizure provoking situations to pharmacological treatment, ketogenic diet and surgical treatment in selected cases. Antiepileptic drugs (AEDs) remain the mainstay in treatment. Effective drugs have been available since the 1850's when bromide was first introduced. The treatment is prophylactic aiming at reducing or ideally eliminating the risk of further seizures as long as the treatment is maintained. Patients are taking their medication daily, often several times a day, for as long as they are considered to be at risk of having seizures. This means in general for several years, and often lifelong. Drug treatment is individualized. The AED is selected according to the patient's type of seizures and epilepsy and other individual characteristics. Also the drug dosage is

individualised. Treatment is often initiated with a low starting dose, which is gradually increased if necessary to obtain seizure control. The aim is to titrate the patient to the lowest effective dosage with freedom from seizures without embarrassing adverse effects.

1.5.2 Pharmacological treatment

Introduced in 1912, phenobarbital is still one of the most frequently used AEDs, and in less affluent societies probably the most cost-effective treatment alternative (47, 48). Phenytoin was discovered in 1939 as the first AED developed based on animal experiments. It is still a drug of first choice in many countries (51) although its saturation kinetics is a clear drawback. Carbamazepine, synthesized in 1953, is still in most countries regarded as the drug of choice for partial and tonic-clonic seizures (51). Valproate, whose anticonvulsant property was recognized serendipitously in 1963, is effective over the complete range of seizures. Valproate is considered a drug of choice for all types of generalized seizures (51).

A number of newer generation AEDs have been introduced during the last 20 years include gabapentin, felbamate, oxcarbazepine, lamotrigine, levetiracetam, tiagabine, topiramate, vigabatrin, and zonisamide (52).

Although the newer AEDs sometimes offer valuable alternatives to the older generation AEDs in special situations, none has proven more effective than the older drugs (53, 54). As in addition the newer drugs are considerably more expensive they have not replaced older AEDs such as carbamazepine, valproate or phenytoin. Due to its low cost, phenobarbital is a reasonable choice in many developing countries, and has also proven effective in such settings (47, 48).

1.5.3 Traditional methods of epilepsy treatment in Vietnam

Treatment for epilepsy in Vietnam followed the fundamental rules of traditional Chinese medicine, which employed herbal drugs, acupuncture, and/or massage to bring upon a balanced functioning of the yin and yang and the five elements within the body. In order to live a long and healthy life, one must live according to the principle of Yin and Yang, i.e. to be orderly and harmonious in the areas of eating, living, and sex so as to maintain proper vitality (7).

Treatment of epilepsy depends on a classification of the illness within the context of traditional Chinese medicine, which is very different from modern Western medicine (9). According to Lai and Lai (10), the first authoritative classification attempted to use age of onset to define two types of seizure, with the age of 10 as the cutting point. Subsequent classification used the degree of resemblance of epileptic cry with animal cry. "Yang (sheep/goat)-Dian-Feng" is one of the commonest colloquial expressions of epilepsy. It has been a common belief among laymen that the onset of epilepsy is linked to the consumption of sheep or goat meat while the mother was pregnant with the patient. This belief may have a connection with a form of intervention for epilepsy called "Mai Xien, "which is to bury a piece of goat intestine into the acupuncture points. At present, the classification system has not been unified and different systems are in use. For example, epilepsy could be presented in three forms: stagnation of wind-phlegm, blood stasis in the cerebral vessels, and accumulation of liver-fire and phlegm-heat (8).

Zhang (55) reported about 200 different prescriptions of herbs claimed effective for treating epilepsy. Wang (56) also reported a herbal drag called Zhenxianling (anti-seizure agent) that he developed to treat epilepsy by supplementing Qi to refresh the brain, removing toxic materials to resolve masses, promoting blood circulation to resolve stasis, and purging fire to eliminate the excessive heat. This drug was made of multiple herbs and other naturally occurring materials.

1.5.4 Special aspects on drug treatment in Vietnam

Studies on the quality and availability of AEDs in Vietnam (57, 58) showed that in the cities and central areas, the availability of AEDs was reasonably good. Four different AEDs (carbamazepine, phenytoin, valproate, and diazepam) from the 12th WHO essential drugs list were available in the majority (57%) of pharmacies (57). Phenobarbital is strictly regulated and could not be obtained in the pharmacies even with a prescription, but was only available from hospitals. The least-expensive AED in pharmacies was carbamazepine. Its daily cost was approximately 0.1 Euro. An average monthly salary for a Vietnamese working in the public health sector is about 24 Euro. The cost of this, the least expensive treatment thus represents >1/10 of the salary. Therefore this product remains expensive and not affordable for poorer individuals (57).

The length of the AED treatment dispensed by the pharmacies varied from 1 day to 1 month depending on the patient's health status and financial situation. In half of the cases, the length of time covered by the dispensed medicines was between 1 and 7 days, which is very a short period, considering the illness. These observations highlight the problems of accessibility and sustainability of drugs for the treatment of a chronic disease such as epilepsy (57).

Furthermore, the AEDs were found to be on display in the windows of many of the surveyed drugstores in Vietnam. They were overexposed to heat and humidity and dissolved badly. Confronted with poor quality, patients' confidence in the treatment may be jeopardized (58).

1.5.5 General health care organization

Vietnam is situated in the South East of the Asian Continent. Vietnam is composed of 63 cities and provinces covering an area of 329,314 km^2. There are 64 races living together, of which Kinh people is the majority. The population is 86.2 million inhabitants with a current annual population growth of 1.33%. General characteristics of the Vietnamese population include: An age distribution in favour of youth (over 90% people under 60 and 20% under 15 years), majority living in rural areas (73%), agriculture playing an important role in economy (53% of GDP). Although there is improvement in quality of life, the hygienic condition in rural areas is still bad with the shortage of running water. Consequently, the rate is high of contagious diseases such as tuberculosis, malaria, meningitis, cysticercosis, which are still frequent causes of epilepsy. The infant mortality rate (under 1) year 2008 is 1.2% and the life expectancy of Vietnamese people is 73 years for females and 68 for males. The average income of Vietnamese is about 40 US dollars per month, but with big differences between people living in cities, rural areas or mountainous areas.

FIGURE 1. Map of Vietnam

Since 1986, the Vietnamese Ministry of Health has established a primary health care system for the whole country to cover basic health care services and public health. Private health care services were officially recognized in Vietnam in 1989. It was firmly controlled by the central government twenty years ago, but over time the ability of the Ministry of Health to shape activities has diminished significantly, due to the growth of the private sector, the larger role of out-of-pocket expenditures, and the ongoing process of fiscal decentralization. The proportion of physicians active in the private sector is between 28-56% in the whole country and as high as 90% in Ho Chi Minh City (59).

The economic growth and subsequent drops in poverty have important consequences for the health financing reforms. The government is becoming more able to financially sustain the expansion of health insurance to formerly uncovered groups (60). School children were made a

priority for enrolment with parents currently pay VND 50,000 (equivalent to US$ 5) for an annual policy for their child. The state voluntary health insurance scheme specifically targets school children, dependants of members of the compulsory scheme, workers in private enterprises with less than 10 employees, the self-employed (e.g. farmers) The scheme covered 3.8 million people at the end of 1997. Ensor (61) suggests that given the experience of other countries at a similar stage of development, compulsory insurance is unlikely to cover more than 10% of the population. The reasons for this include a low proportion employed in the formal sector, the high rural population, and low incomes (61).

Like other countries in the South-East Asian region, Vietnam is undergoing an epidemiologic health transition. Chronic disorders and health problems of aging populations are increasing. Further training to strengthen the quality of community-level care for adult chronic diseases is needed. Seventy per cent of commune health centres staff responsible for internal medicine and 96% of private health care providers were unable to identify half the essential questions to be asked of a patient with hypertension (62).

1.5.6 Organization of care for epilepsy in Vietnam

Mental health service in Vietnam has set up a network of community-based mental health centres, which have been given the primary responsibility to provide care for people with epilepsy in the community. Only those with more refractory epilepsy are referred to the relatively few neurologists in the country (63). It is presently unclear to what extent patients with epilepsy in general are actually consulting the community-based mental health care service, the family doctor or others.

In terms of technical equipment for diagnostic work-up, most cities and provinces have access to digital EEG and CT-scanners. There are several MRI equipments in each of the big cities Ha Noi, Ho Chi Minh City, Hue, and Da Nang. In rural or remote areas, there is a shortage of equipments necessary for diagnosing and managing epilepsy patients. There is no laboratory for therapeutic drug monitoring of AEDs in the country.

The treatment of epilepsy is based mostly on pharmacological therapy with the conventional medications such as phenobarbital, phenytoin, carbamazepine or diazepam for acute treatment. According to the national programme for the treatment of epilepsy, phenobarbital and phenytoin are provided free of charge to epilepsy patients. However, the drugs are available through this programme only from local health centres in charge of the epilepsy management and AEDs are dispensed for 10 days at a time. As a consequence, AEDs are accessible through the programme only with regular and frequent visits to the physician. The newer generation medications such as gabapentin, levetiracetam, topiramate and lamotrigine are not covered by medical insurance and thus not affordable for poor people with epilepsy. Other treatment modalities such as epilepsy surgery, ketogenic diet, vagus nerve stimulation have not been applied yet in the country.

1.5.7 Public Attitudes

Public understanding and attitudes towards epilepsy, patients' concepts of disease, and help-seeking behaviour are all important components with an impact on the management and lives of

people with epilepsy. Such information is also missing and much needed, as is information on to what extent people with epilepsy have access to and take medication.

2 AIMS

Much essential data for the design and implementation of an effective management programme for people with epilepsy is lacking in Vietnam as in most other Asian countries. This includes basic epidemiological information on the incidence and prevalence of epilepsy, and on risk factors and etiologies. Thus, the overall objective of this project, Epidemiology and Care of Epilepsy in Ba Vi (EPIBAVI), was to provide essential epidemiological data on epilepsy from a representative rural district in Vietnam, and thus a basis for a future management of people with epilepsy in Vietnam

The specific aims were

- *To study knowledge attitudes and practice(KAP) toward epilepsy in Ba Vi, Vietnam*
- *To study the prevalence of epilepsy in Ba Vi, Vietnam*
- *To study the treatment gap of epilepsy in Ba Vi, Vietnam*
- *To study the incidence of epilepsy in Ba Vi, Vietnam*

3 METHODS

3.1 SETTINGS

The research on "Epidemiology and Care of Epilepsy in Vietnam" was carried out in an Epidemiological Field Laboratory (FilaBavi) in the Ba Vi district, which is located in the Ha Tay province, 60km west of Hanoi – the Capital of Vietnam. The district covers 410 km2 with different types of geographic characteristics from lowland, highland to mountainous areas. The population is 235,000 people with different ethnic groups: King 91%, Muong 8%, Dao, Tay, Hoa and Khmer (64). The average annual income expressed as rice production is 290 kilograms/person/year (approximately equivalent to US$ 40/person/year), (64). The crude mortality rate is estimated to 5.1 per 1,000 person/year (4.7 for female and 5.6 for males) (65). The area is considered to be representative of rural Vietnam.

The health care system in the district is organized according to the national pattern with one district hospital with 150 beds and 32 communal health centres. There are also private consultants including doctors, traditional healers, and drug-sellers. Established in 1997, FilaBavi is based on 69 clusters (households and villages) out of 352 clusters. Stratification was implemented based on geographical area types (lowland, highland, island and mountainous areas). The total number of households in the 69 clusters was 11,547 with 49,893 inhabitants in the year 2000. In 2005, 12,960 households with 48,911 inhabitants were covered by these 69 clusters. A longitudinal epidemiological surveillance system has been established in this district through quarterly door-to door surveys of all persons within the clusters (64). In the surveillance system, information on demographic events, health related conditions and use of health services is collected every 3 months by trained surveyors.

FilaBavi has an established quality control where "spot checks" by field supervisors are conducted to witness the interviews on approximately a 5% sample of the home visits per cycle. Field co-ordinators and researchers conduct random re-interviews on approximately 10 household visits per week. All completed questionnaires are reviewed by the FilaBavi office staff before sending to computer keyers. A computer checking programme has been designed to automatically detect inconsistencies while entering data.

3.2 DEFINITIONS

The following definitions are mainly based on the suggestions made by the ILAE Commission for studies on the epidemiology of the epilepsies (20).

Epilepsy
A condition characterized by two or more unprovoked epileptic seizures. An episode of status epilepticus or multiple seizures occurring in a 24-hour period were considered as single events.

Active epilepsy
A person fulfilling criteria for epilepsy and with at least one unprovoked epileptic seizure in the previous 5 years or ongoing pharmacological treatment for epilepsy.

Provoked seizures (acute symptomatic seizures)

Seizures occurring in close temporal relationship to acute systemic, metabolic or toxic disturbance or in connection with an acute CNS insult (e.g. stroke, CNS-infection, brain trauma, intracranial bleeding) (66).

Symptomatic epilepsy
Repeated unprovoked seizures caused by a known underlying condition leading to a static (e.g. previous, >7 days old, stroke or traumatic brain injury or CNS infection after the active phase) or slowly progressive (e.g. brain tumour or dementia) CNS lesion.

Cryptogenic epilepsy
Repeated unprovoked seizures for which an underlying lesion is suspected, the exact nature of which has not been determined.

Idiopathic epilepsy
Certain established partial or generalized epilepsies without underlying etiology and with genetic background, e.g. absence epilepsy, juvenile myoclonic epilepsy, benign epilepsy of childhood with centro-temporal spikes.

Presumed etiology
A condition preceding seizure onset, known to be an etiological factor for epilepsy, and compatible with the type seizures/epilepsy of the case in question.

Prevalent case:
A person with active epilepsy at time of survey.

Incident case:
A person with onset of epilepsy within one year prior to the date of screening or clinical examination.

Incidence rate:
Number of incident cases per 100,000 person-years.

Treatment gap:
Number of people with active epilepsy not on adequate treatment, expressed as percentage of the total number with active epilepsy (21). Adequate treatment was defined as regular use of an established AED (any older or newer generation) at the time of the survey, irrespective of type of AED in relation to seizure classification.

3.3 STUDY DESIGNS

3.3.1 Knowledge Attitudes and Practice toward Epilepsy (Paper I)

Study population
Of the 48,911 residents, 2,005 persons aged 19 to 71 years (933 males) were selected to participate in the survey, which was conducted from January to April 2005 in two stages. First, households were selected randomly, and then one person was randomly selected in each household. If the selected person was unable to answer the questions either because of mental

retardation or unavailable due to migration out of the region, he or she was replaced with a backup subject that was also randomly selected. Background demographic data were obtained from the FilaBavi database with information on education, occupation, marital status, family and residence.

Survey instrument
We utilized a questionnaire previously used in several similar studies including demonstration projects of the Global Campaign (33). The English version of the questionnaire was translated into Vietnamese and retranslated into English to confirm the accuracy of the translation. This questionnaire was applied by 46 trained interviewers during door-to-door surveys of the households, where the respondents were interviewed individually in their home.

3.3.2 The prevalence and the incidence of epilepsy (paper II and paper IV)

Study populations
We carried out two surveys three years apart using the FilaBavi infrastructure. The first survey was performed from January to December 2005 and the second from June to December 2008. The first was a combined survey to identify prevalent and incident cases of epilepsy. In both surveys, residents aged 1 year or more in the same 69 clusters of FilaBavi were screened for the possible existence of epilepsy. A total of 48,080 persons were eligible for the first survey, out of which 811 (1.7%) were unreachable or unwilling to participate. This proportion was similar in the second survey, 864 out of 49,832 eligible (1.7%). Thus, 47,269 persons from 12,960 households (year 2005) and 48,968 persons from 14,137 households (year 2008) were questioned in their homes by interviewers in conjunction with the regular survey. Parents were interviewed concerning children under 15 years and the closest relative in the household concerning people with disabilities preventing them from responding accurately.

Screening questionnaire
We used a screening questionnaire for the epidemiology of epilepsy developed by the WHO for the demonstration projects of the Global Campaign (34). The questionnaire consists of 13 questions that were translated to Vietnamese and retranslated to English to confirm the accuracy of the translation. This questionnaire has previously been validated in other countries with a sensitivity approaching 100% and a specificity close to 80% (35).

Verification of diagnoses
All individuals with a positive response to any of the screening questions were assessed by a Vietnamese neurologist from the research team. A few patients who were screened negative self-referred, and were included in the clinical examination for confirmation of diagnosis. The clinical examination included a medical history, and comprehensive physical and neurological examination carried. All persons fulfilling the criteria for new onset epilepsy were offered an EEG.

After completion of the second screening and case validation, all incident cases from both surveys were offered a CT-Scan of the brain.

The diagnosis of epilepsy was made by the neurologist responsible for assessment of the patient. Difficult cases were discussed among the neurologists in the project group and decision made

by consensus. Seizures and the type of epilepsy or epilepsy syndrome were classified according to the 1989 recommendations of the ILAE (15). Cases with generalized tonic-clonic seizures without auras or other focal symptoms or signs, without epileptiform activity on EEG, and with no known underlying etiology were classified as epilepsies without unequivocal generalized or focal features. The etiological classification was based on the medical history and clinical examination supplemented by results of the CT-scan.

Data on education, marital status, residency and household economy were obtained from the FilaBavi database.

3.3.3 The treatment gap of epilepsy (Paper III)

Study population
Out of 206 persons with active epilepsy identified in Paper II, 189 were interviewed about their treatment by trained interviewers during door-to-door surveys from December 2007 until February 2008. Seventeen of the 206 were unavailable for the interview because of migration or for other reasons. Parents provided answers for children less than seven year of age. The semi-structured interviews inquired about current and previous treatment for epilepsy.

Definitions
The treatment gap is defined as the number of people with active epilepsy not on treatment or on inadequate treatment, expressed as a percentage of the total number with active epilepsy (21). Information was also obtained on use of traditional Chinese or Vietnamese medicine.

3.4 QUESTIONNAIRES

We utilized the following questionnaires for our studies:

3.4.1 KAP questionnaire (Paper I).

1. Have you ever heard of or read about the disease called epilepsy?
2. Did you ever know anyone who had epilepsy?
3. Have you ever seen anyone who was having a seizure?
4. Would you object to having any of your children in school or at play associate with persons who sometimes had seizures?
5. Would you object to your son or daughter marrying a person who sometimes had seizures?
6. Do you think people with epilepsy should be employed in jobs like other people?
7. Do you think epilepsy is a form of insanity?
8. What do you think is the cause of epilepsy?
9. What do you think an epileptic attack is?
10. If your relatives or friends have epilepsy, what kind of treatment would you suggest?

3.4.2 Screening questionnaire for prevalence and incidence of epilepsy (Papers II and IV).

1. Have you ever had attacks of shaking of the arms or legs which you could not control?
2. Have you ever had attacks in which you fall and become pale?

3. Have you ever lost consciousness?
4. Have you ever had attacks in which you fall with lost consciousness?
5. Have you ever had attacks in which you fall and bite your tongue?
6. Have you ever had attacks in which you fall and lose control of your bladder?
7. Have you ever had brief attacks of shaking or trembling in one arm or leg or in face?
8. Have you ever had attacks in which you lose contact with the surroundings and experience abnormal smells?
9. Have you ever been told that you have or had epilepsy or epileptic fits?
10. Have you ever had attacks in which you lose contact with your surroundings and experience a sensation in which objects change shape or size?
11. Did you ever have attacks of convulsions in fever before the age of 5?
12. Have you ever suddenly in a daze or amazement, lost something from your hand during an activity, writing or eating?
13. Have you ever had suddenly in a daze, purposeless activity of hands of which you subsequently have no memory?

3.4.3 Questionnaire for treatment gap (Paper III)

1. Do you regularly take any type of preventive medication for your epilepsy?
2. Please describe type of medication
    a. AED
    b. Traditional local medicine
    c. Other
3. What kind of AED do you use?
4. Who advised you to take this treatment
    a. Medical doctor
    b. Other health staff including drug sellers (specify)
    c. Relatives/friends
    d. None, decided by myself
5. How do you take your treatment
    a. Daily
    b. Periodically (for weeks or months)
    c. Occasionally, in relation to seizures
    d. Other pattern
6. Do you take any type of treatment for epilepsy recently?
7. Do you take any type of treatment for epilepsy yesterday?
8. Do you take any type of treatment for epilepsy today?
9. How long have you been taking your treatment?
10. Have you experienced any unwanted effects of the treatment you take
11. How do you perceive the effectiveness of the treatment you take?
    a. Good
    b. Fair
    c. Poor

For those who previously taken AED but stopped:

12. For how long did you take your medication?
13. Why did you stop taking your medication?

3.5 EEG AND CT-SCAN

3.5.1 EEG protocol.

Digital EEGs were recorded at different health care centres using a portable EEG equipment. Recordings were made during rest for at least 10 minutes with 5 eye openings, and during hyperventilation for 3 minutes with an additional 2 minutes at rest. The 19 scalp electrodes were placed according to the International 10-20 system, and one or two reference electrodes placed at mid-frontal and mid-parietal position. All electrodes had impedances less than 20 kOhm and a recording standard was used with an amplification of 100 microV and with low and high filter set at 0.5 and 70 Hz, respectively. Notch filter was used when necessary. The EEG signals were fed and stored in a personal computer using the Nervus EEG system (Nervus 3.4 Viasys NIC nEEG). The findings were classified into one of the following five groups: No abnormality (1); epileptiform abnormality of generalized (2) or focal character (3); and non-epileptiform abnormality with generalized (4) or focal (5) distribution.

3.5.2 CT protocol.

The CT-scan utilized the Routine Brain Asteion Protocol and Iodine contrast was used for patients above 5 years.

TABLE 1. Routine Brain – Asteion Protocol

Position	Supine, head first
Topogram Direction	Cranio caudal
Scan Type	Axial
KV/mA	120 kv/ 150 mA
Slice Thickness	5 mm Infratentorial x 7mm Supratentorial
Intervall	5 and 7
Scan Start/End location	Skull base – Skull vertex
FOV	24 mm
Direction	OM
IV Contrast Type/ Volume/ Rate	Telebrix 350/ 50 ml/ 2ml/s

3.6 DATA MANAGEMENT AND STATISTICS

Data processing was conducted on four networked computers in the hands of one data manager and three data entry clerks. The software used was a custom designed database in MS Access. Each of the surveyed individuals and household has a unique code that is constant for all the FilaBavi studies. Our study also utilized this code and could access the database of other studies as well as to that of the demographic surveillance system. All analyses were performed using STATA for Windows version 9.1.

Chi2 test, and Fisher's exact test whenever appropriate, was used to analyze the association between background socio-demographic (age group, sex, education, marital status, occupation, geographical region) and responses to questions relating to familiarity with epilepsy and attitude towards epilepsy in KAP study and the treatment gap proportion in treatment gap study. 95% confidence interval of the treatment gap was also calculated.

Prevalence and incidence rate and its 95% confidence interval were calculated by age and sex and were also standardized by age using direct standardization method based on the standard world population year 2000 (67). Internal comparisons between socio-demographic groups were performed adjusting for age.

All statistical tests were two-sided and differences with p value < 0.05 were considered as statistically significant.

3.7 ETHICAL APPROVAL

The studies were approved by the local authority of the Ba Vi district and by the Ethical Committee of the Hanoi Medical University. All respondents gave informed consent for participation in the study.

4 RESULTS

4.1 KNOWLEDGE ATTITUDES AND PRACTICE TOWARD EPILEPSY AMONG ADULTS IN BA VI, VIETNAM (PAPER I)

Purpose

To assess knowledge, attitudes and practice toward epilepsy in a population based study in a rural district of Vietnam.

Results

Responses to questions about familiarity with epilepsy are summarized in Table 2. Out of the 2,005 respondents, 67% had heard about epilepsy, 52% had known someone with seizures and 49% had witnessed seizures. Younger age groups and singles were significantly less likely to have heard or read about epilepsy and also less frequently knew someone with epilepsy. Younger people, singles and females were also less likely to have seen an epileptic seizure. Attitudes toward epilepsy by different groups of respondents are given in Table 3. In total, 36% would object to their children playing with someone with seizures and 82% to their children marrying someone with epilepsy. Only 33% thought that epilepsy patients should be employed in a job as other people while10% thought that epilepsy was a form of insanity. Younger people were less likely to object to their children playing with others with seizures. Half of the respondents (50%) thought epilepsy was caused by a brain disease and 80% would suggest consultation of a medical doctor for epilepsy. Familiarity with epilepsy, having heard of epilepsy, known someone with, or having seen seizures was associated with less negative attitudes.

Conclusions

Knowledge of epilepsy among Vietnamese people is still limited compared to some Western countries and the attitudes more negative. Our findings indicated more negative attitudes also in relation to another recent survey from Vietnam. This discrepancy may be due to differences in socio-demographic characteristics and educational level of the study populations.

TABLE 2. Responses to question about familiarity with epilepsy

Age Group	Total n (%)	Heard about epilepsy Yes (%)	Know someone with seizure Yes (%)	Have seen seizures Yes (%)
19 – 24	360 (18%)	52.8	24.2	22.2
25 – 34	452 (22.5%)	66.4	49.3	47.3
35 – 44	511 25.5%)	69.3	59.5	51.5
45 – 54	372 18.6%)	74.7	65.1	64.8
55 – 64	190 (9.5%)	69.5	57.9	60.5
65 – 71	120 (6%)	75.0	65.0	63.3
Sex				
Male	933 (46.5%)	67.8	53.7	53.1
Female	1072 (53.5%)	66.3	50.7	46.1
Education				
Illiterate	37 (1.8%)	67.6	37.8	54.1
Primary	415 (20.7%)	64.1	47.2	47.2
Secondary, higher	1553 (77.5%)	67.8	53.7	49.8
Occupation				
Employee	245 (12.2%)	62.9	51.4	54.7
Farmer	1401 69.9%)	68.3	54.2	48.9
Other [(1)]	359 (17.9%)	64.9	44.0	47.4
Marital Status				
Single	341 (17%)	54.0	28.2	26.4
Married	1544 (77%)	69.8	57.1	53.6
Other [(2)]	120 (6%)	68.3	55.0	59.2
Geographic				
Mountainous	497 (24.8%)	56.1	54.3	44.5
Plain	1508 (75.2%)	70.6	51.3	50.9

(1): Student (n=51), trader (n=99), carpenter/craftsman/serviceman/bricklayer/other (n=209 altogether).
(2): Divorced (n=14), widow (n=94), separated (n=12).

TABLE 3. Responses to questions about attitudes toward epilepsy

		Object to children playing with others with seizures	Object to children marrying person with seizures	Employment like others for subject with epilepsy	Epilepsy is a form of insanity
Age Group	Total n (%)	Yes (%)	Yes (%)	Yes (%)	Yes (%)
19 – 24	360 (18%)	29.2	70.8	31.1	7.8
25 – 34	452 (22.5%)	41.8	83.2	32.3	9.3
35 – 44	511 25.5%)	32.9	85.1	35.6	11.2
45 – 54	372 18.6%)	38.2	84.1	32.3	9.7
55 – 64	190 (9.5%)	42.1	86.8	35.8	9.5
65 – 71	120 (6%)	36.7	84.2	20.8	16.7
Sex					
Male	933 (46.5%)	34.0	80.7	33.9	11.4
Female	1072 (53.5%)	38.3	83.2	31.4	8.9
Education					
Illiterate	37 (1.8%)	35.1	83.8	35.1	5.4
Primary	415 (20.7%)	38.6	80.7	29.4	9.4
Secondary and higher	1553 (77.5%)	35.7	82.4	33.4	10.3
Occupation					
Employee	245 (12.2%)	36.7	84.5	35.1	6.5
Farmer	1401 69.9%)	37.3	80.9	32.5	10.8
Other[(1)]	359 (17.9%)	32.0	85.0	30.9	9.5
Marital status					
Single	341 (17%)	30.8	71.8	28.2	7.3
Married	1544 (77%)	36.8	83.9	34.1	10.6
Other[(2)]	120 (6%)	45.8	87.5	25.8	10.8
Geographic					
Mountainous	497 (24.8%)	36.4	79.7	53.3	5.4
Plain	1508 (75.2%)	36.3	82.8	25.7	11.5

(1): Student (n=51), trader (n=99), carpenter/craftsman/serviceman/bricklayer/other (n=209 altogether).

4.2 THE PREVALENCE OF EPILEPSY IN A RURAL DISTRICT OF VIETNAM (PAPER II)

Purpose

To study the prevalence of active epilepsy in people 1 year or older in a rural district of Vietnam.

Results

The screening procedure is depicted in Figure 2. Out of 47,269 screened, 1,338 (2.8%) had a positive response to the questionnaire. Of these, 206 fulfilled the criteria for active epilepsy after clinical examination. The prevalence by age and sex is presented in Table 4. The age-adjusted prevalence was 4.4 per 1,000 (95%CI 3.8-5.0), higher among males, 5.1(4.1-5.9), than females, 3.8(3.0-4.6). The prevalence by socio-demographic conditions is given in Table 5. The prevalence was higher among those with lower compared with higher education and among single compared with those married.

EEG was without abnormalities in 78% of the investigate epilepsy cases and revealed epileptiform activity in 11% (n=21). A presumed etiology was identified in 33%, with mental retardation (13%) and CNS infections (9%) being the most frequent.

Only 21% of the patients were seizure free the year before the examination (Table 6).

Conclusions

The prevalence of active epilepsy in Vietnam is similar to some other Asian countries but lower than in developing countries from Africa and South America. The risk of having epilepsy is related to socio-demographic conditions.

FIGURE 2: Flow chart describing the screening process for the prevalence study from January to December 2005

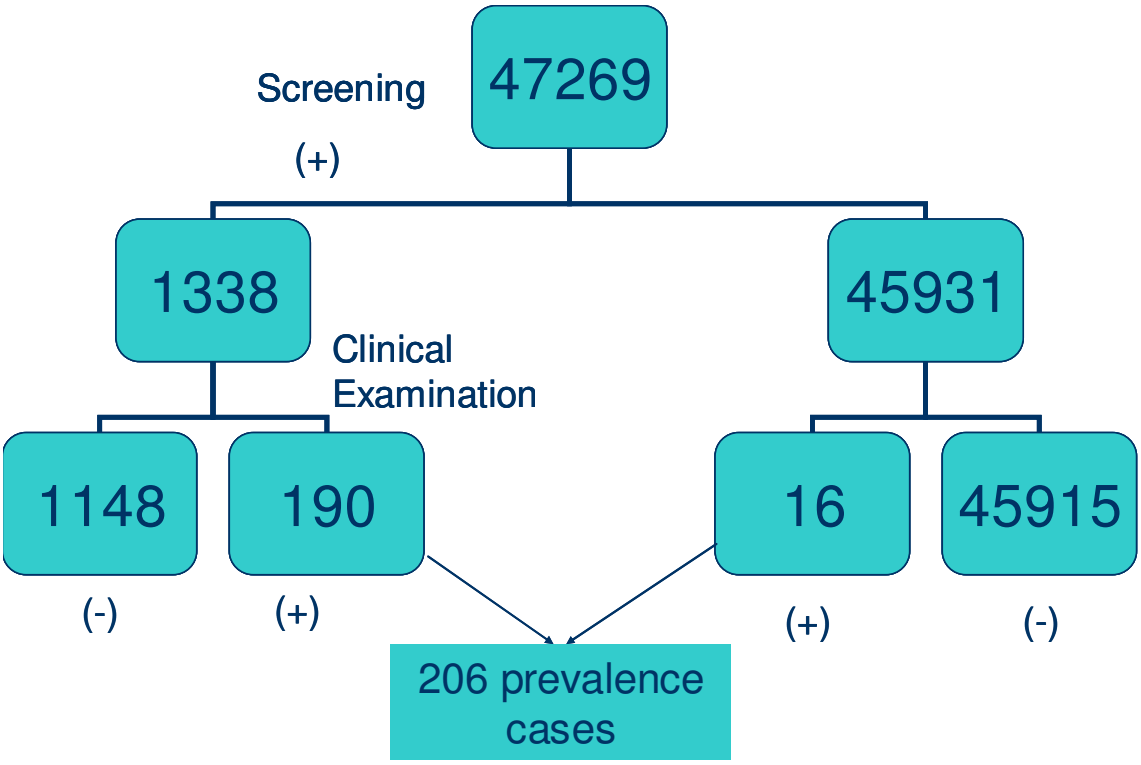

TABLE 4. Prevalence of active epilepsy in Ba Vi, Vietnam by age and sex.

	Male			Female		
Age group	Pop.	N	Prev/1000 (95%CI)	Pop.	n	Prev/1000 (95%CI)
1-10	4079	28	6.9 (4.3 – 9.4)	3807	25	6.6 (4.0 – 9.1)
11-20	5181	26	5.0 (3.1 – 6.9)	5018	14	2.8 (1.3 – 4.2)
21-30	3655	17	4.7 (2.4 – 6.9)	3825	15	3.9 (1.9 – 5.9)
31-40	3146	15	4.8 (2.4 – 7.2)	3317	17	5.1 (2.7 – 7.6)
41-50	3210	15	4.7 (2.3 – 7.0)	3436	12	3.5 (1.5 – 5.5)
51-60	1528	10	6.5 (2.5 – 10.0)	1785	1	0.6 (0.0 – 1.7)
61-70	1045	1	1.0 (0.0 – 2.8)	1367	4	2.9 (0.0 – 5.8)
>70	890	3	3.4 (0.0 – 7.2)	1980	3	1.5 (0.0 – 3.2)
Total	22619	115	5.1 (4.1 – 6.0)	24443	91	3.7 (3.0 – 4.5)

TABLE 5. Prevalence of active epilepsy in adults in Ba Vi, Vietnam, by socio-demographic conditions

Educational level (*)	pop	N	Prevalence/1000 (95%CI)	Age adjusted prevalence/1000 (95% CI)
Illiterate	58	-	-	-
Primary (1)	5,331	33	6.2 (4.1 – 8.3)	9.6 (5.8 – 13.4)
Secondary, higher	28,842	99	3.4 (2.6 – 4,1)	3.3 (2.7 – 4.0)
Total	34,231	132	3.9 (3.2 – 4.5)	
Marital Status (*)				
Single	7,018	51	7.3 (5.3 – 9.3)	17.7 (10.6 – 24.8)
Married	23,681	69	2.9 (2.2 – 3.6)	2.4 (1.8 – 3.0)
Other (divorced, separated, widow)	3,548	12	3.4 (1.5 – 5.3)	6.4 (5.0 – 12.5)
Total	34,247	132	3.9 (3.2 – 4.5)	
Geographic region				
Mountainous	11,583	34	2.9 (2.0 – 3.9)	2.9 (1.9 – 3.9)
Plain	35,686	172	4.8 (4.1 – 5.5)	4.9 (4.1 – 5.6)
Total	47,269	206	4.4 (3.8 – 5.0)	
Economic status (*)				
Low income (2)	17,334	80	4.6 (3.6 - 5.7)	4.7 (3.6 – 5.7)
High Income (3)	18090	54	3.0 (2.2 – 3.8)	3.0 (2.2 – 3.8)
Total	35,424	134	3.8 (3.1 – 4.4)	

*: Age equal and above 15.

1. Primary: Class 1 to class 6
2. Low income: total income of the household equal or less than 16.9 million VND/year
3. High income: total income of the household greater than 16.9 million VND/year

TABLE 6. Seizure control from the year before the date of clinical examination in patients with active epilepsy by age and sex

	Seizure control	
Sex	Number of case	Seizure free, n (%)
Female	91	16 (17.6)
Male	115	27 (23.5)
Age group		
1-15	74	26 (35.1)
16-45	99	13 (13.1)
>45	33	4 (12.1)
Total	206	43 (20.9)

4.3 THE TREATMENT GAP OF EPILEPSY IN A RURAL DISTRICT OF VIETNAM (PAPER III)

Purpose

To analyze the treatment gap in people with active epilepsy in a rural district of Vietnam

Results

We analysed the treatment gap by interviewing 189 persons previously identified as having active epilepsy in a population based epidemiological project in a rural district of Vietnam. Only 29 persons were on regular treatment with AEDs at the time of the survey. The treatment gap was thus 84.7% (95%CI: 79.5% - 89.8%). The treatment gap in relation to socioeconomic and clinical characteristics is presented in Table 7. The treatment gap was neither associated with age, gender, education, income, nor seizure control status, but was higher among those living single compared to married ($p<0.05$). The most common reason for not taking AEDs expressed by patients who never tried, as well as among those who tried but discontinued AEDs, was the perception that their seizures were too few to justify the trouble and costs associated with treatment.

Conclusions

Only approximately 15% of people with active epilepsy in the present study were on adequate treatment with AEDs despite a national programme providing some AEDs free of charge.

TABLE 7. Patients on and without current adequate antiepileptic drug (AED) treatment in relation to socioeconomic and clinical characteristics.

	On AED	*Without AED*	*Treatment gap %*	*p-value* [1]
Age Group				
1 – 15	4	53	93.0%	p>0.05
16 – 45	18	77	81.0%	
>45	7	30	81.1%	
Gender				
Male	16	90	84.9%	p>0.05
Female	13	70	84.3%	
Education				
Illiterate or too young	3	23	88.5%	p>0.05
Primary	8	50	86.2%	
Secondary, higher	18	87	82.9%	
Occupation				
Farmer	11	55	83.3%	p>0.05
Other	18	105	85.4%	
Marital Status				
Single	15	113	88.2%	P<0.05
Married	14	47	77.0%	
Geographic				
Mountainous	2	32	94.1%	p>0.05
Plain	27	128	82.6%	
Income				
Low income [2]	19	99	83.9%	p>0.05
High income [3]	10	61	85.9%	
Epilepsy Classification				
Localization related symptomatic epilepsy	7	30	81.1%	P<0.05
Localization related cryptogenic epilepsy	15	47	75.8%	
Generalized idiopathic epilepsy	1	12	92.3%	
Unequivocal generalized or focal epilepsy	6	71	92.2%	
Seizures free during the year preceding survey [4]				
Yes	3	35	92.1%	p>0.05
No	26	118	81.9	

[1] Fisher exact test was used if expected frequencies less than 5.
[2]. Low income: total income of the household equal or less than 16.9 million VND/year.
[3]. High income: total income of the household greater than 16.9 million VND/year.
[4] 7 cases were excluded because of missing data.

4.4 THE INCIDENCE OF EPILEPSY IN A RURAL DISTRICT OF VIETNAM (PAPER IV)

Purpose

To study the incidence and etiology of epilepsy in people 1 year or older in a representative rural region of Vietnam.

Results

The screening procedure is depicted in Figure 3. On the first survey 2.8% screened positive according to the questionnaire. Of these, 19 had epilepsy onset within 1 year preceding the screening, yielding an incidence rate of 40.2/100,000 (95%CI 22.1-58.3). On the second survey 1.8% were screened positive, 21 of these had epilepsy onset within 1 year preceding the screening, giving an incidence rate of 42.9/100,000 (95%CI 24.5-61.2). The age-adjusted incidence was 44.8/100,000 (95%CI 30.6-59.0). The incidence rate by age and sex of the two surveys combined is summarized in Table 8. Table 9 gives incidence rates by socio-demographic conditions. The incidence was higher in those under 16 years, among people with lower education, and with lower income. CT-scan was performed in 29 cases and only 2 cases were found with some abnormalities. A presumed etiology was identified in only 7 out of 40 cases and none had signs of neurocysticercosis. .

Conclusions

The incidence rate of epilepsy in rural Vietnam in our study was lower than in developing countries in Latin America and Africa and similar to rates in Europe and North America. The association with socio-economic conditions was similar to the patterns reported from Europe and North America.

FIGURE 3. Flow charts describing the selection process in the two screenings for epilepsy. First screening from January to December 2005 (upper panel) included also screening for prevalent epilepsy cases. Second screening from June to December 2008 (lower panel).

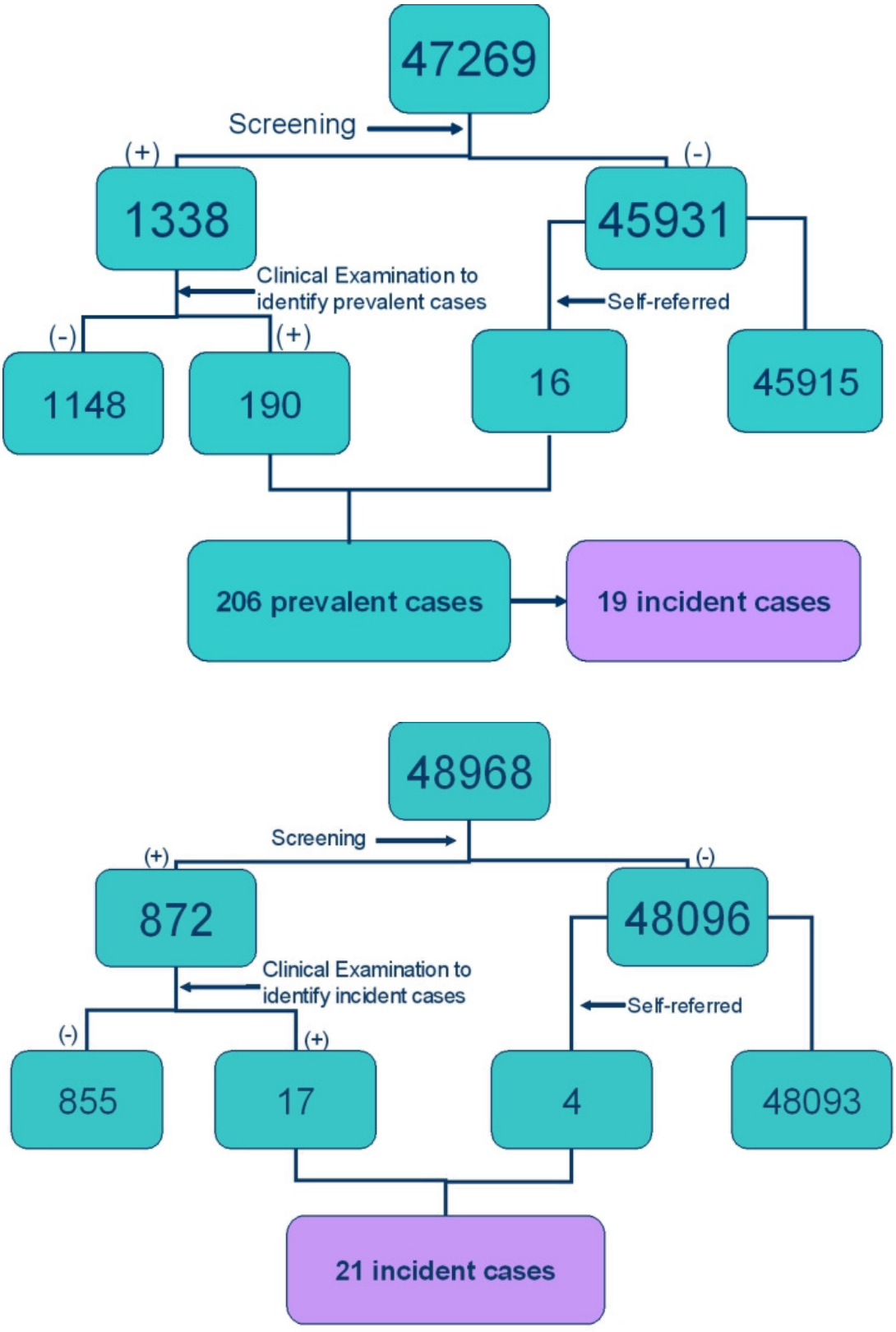

TABLE 8. Incidence rate per 100,000 person years and 95% confidence intervals (CI) of new onset epilepsy in Ba Vi by age and sex. Data from two surveys carried out 2005 and 2008 are combined.

Age	**Male**			**Female**			**Total**		
Years	N	IR	95% CI	N	IR	95% CI	n	IR	95% CI
1-15	12	93.2	40.5-146.0	12	100.7	43.8-157.7	24	96.8	58.1-135.6
16-50	9	34.8	12.1-57.5	3	11.1	0-23.7	12	22.7	9.9-35.5
>50	4	52.7	1.1-104.4	0	0	0	4	21.5	0.4-42.6
Total	25	53.9	32.8-75.1	15	30.1	14.9-45.3	41	41.6	28.7-54.4

TABLE 9. Incidence rates of new onset epilepsy in Ba Vi by socio-demographic conditions. Data from the two surveys combined.

		N	Incidence rate/100,000 person-years	Age adjusted incidence rate/100,000 person-years
Marital Status	Single	29	61.2 (39.0-83.5)	41.5 (19.6-63.4)
	Married	11	22.5 (9.2-35.8)	15.5 (0.6-25.0)
Education	Primary	20	102.1 (57.4-146.8)	83.1 (31.6-134.6)
	Secondary or higher	10	15.0 (5.7-24.2)	12.7 (0.4-21.3)
Geographic	Mountainous	10	41.9 (16.0-67.9)	46.7 (17.2-76.3)
	Plain	30	41.4 (26.6-56.3)	44.2 (28.0-60.3)
Income	Low Income	27	56.5 (35.1-77.8)	57.7 (35.8-79.7)
	High Income	13	26.9 (12.3-41.5)	31.7 (13.9-49.4)

Cases below school age (n=10) excluded from this analysis

5 DISCUSSION

5.1 METHODOLOGICAL ASPECTS

The major strengths of the present project are firstly that the studies are population-based utilising an established epidemiological field laboratory. A second major strength is the comprehensive approach of the project. We have analysed public knowledge and attitudes toward epilepsy, incidence and prevalence and etiology of epilepsy, as well as the treatment gap, all in the same well characterized representative population from rural Vietnam. A very high participation rate in our surveys is a further strength.

We applied screening instruments that have been utilized before in similar studies in China and several other countries (33, 34). The screening questionnaire for epilepsy has been validated locally and all screened positive had their diagnosis confirmed or refuted through a clinical examination by a neurologist of our team.

In addition, all identified cases with epilepsy were offered an EEG examination and all incident cases an etiological work-up with a CT-scan of the brain. Furthermore, through the FilaBavi infrastructure, we had access to socio-demographic characteristics that could be utilized in our analyses. We believe that this combination makes our study unique among epidemiological projects from developing countries and that we have evaded most of the methodological problems associated with epidemiological studies of epilepsy in developing countries (68).

There are also limitations. In the KAP study (paper I), we included also the 33% who reported not to have read or heard about epilepsy. The value of analyzing attitudes toward epilepsy among such individuals can of course be questioned. However, knowledge is likely to affect attitudes and selective exclusion of the respondents who declare the least familiarity with epilepsy might result in a biased perception of the attitudes in the general population.

Although close to 50,000 individuals were screened in our surveys of prevalence and incidence of epilepsy, the number of identified cases was rather small, in particular in the incidence study. This of course affects the precision of our estimates as reflected in comparatively wide confidence limits. This reduced our possibilities for more refined subgroup analyses and for assessment of associations. The accuracy of the reported prevalence and incidence rates also depends on the sensitivity of our screening method. In addition to validations made in other countries, we applied the questionnaire to 50 patients from Hanoi with established epilepsy, and all were screened positive (paper II). It is nevertheless intriguing that 16 individuals that were screened negative in our first survey self-referred to the clinical examination and were found to have epilepsy. This might be explained by the negative attitudes towards epilepsy revealed in this population in our study on attitudes (paper I). Some patients with epilepsy might be reluctant to disclose the diagnoses to the interviewers. It is also intriguing that the proportion screened positive was different in the two surveys. We have no good explanation for this, except a possible “training effect” among the interviewed. However, it is reassuring that the incidence rates in the two surveys were remarkably similar.

An important weakness of our studies is the lag time from completion of the screening to clinical examination, EEG and in particular CT-scans. Some people may migrate and theoretically also die between screening and clinical examination. However, very few of those screened positive failed to participate in the neurological investigation. The lag time definitely contributed to the fact that a proportion of the incident cases did not undergo CT-scans and this could contribute to an underestimate of symptomatic epilepsies.

5.2 INCIDENCE AND PREVALENCE

5.2.1 Overall incidence and prevalence

The most important observations from our studies are the incidence and prevalence rates of epilepsy in the population of the Ba Vi district. It has frequently been suggested that the prevalence and in particular the incidence of epilepsy is considerably higher in developing countries compared to more economically privileged countries (32, 69). In contrast, our data suggest that these rates are similar in Vietnam, Europe (31, 70), and North America (18, 27, 71). The age-adjusted incidence rate of 44.8/100,000 person-years in our study is also in line with the very limited data available from other Asian countries, e.g. 35/100,000 in India (37). High age-adjusted incidence rates have been reported from Latin America, e.g. 111/100,000 person-years in Chile (22), whereas incidence rates in some African countries have been of the same order as in our study from Vietnam, 51/100,000 in Tanzania (72) and 43/100,000 in Ethiopia (73).

The age-adjusted prevalence of active epilepsy in our study, 4.4/1,000, is close to what has been reported from other countries in Asia (26) and comparable to the rates reported in Europe, 4.5-5.0/1,000 (31). Otherwise, reported prevalence rates based on door-to-door methodology have varied considerably, ranging from 2.2/1,000 in a study from India (74) to 41.0/1,000 in a study from Nigeria (75). In general prevalence rates reported from countries in Africa and in particular Latin America have been considerably higher than in our study (23, 28).

There are no previous Vietnamese studies on the incidence or prevalence of epilepsy that have been published in full. However, one door-to-door survey so far published only in abstract, reported a considerably higher prevalence of 10.7 per 1,000 (39). The discrepancies may be due either to methodological differences or be real possibly related to the high incidence of neurocysticercosis in this other, not yet fully published study. .

5.2.2 Incidence and prevalence by socio-demographic conditions

The incidence was slightly higher in men compared to women in our study in agreement with most other reports from different populations and regions (25, 27, 29, 30, 36-38, 70, 73, 76-81). Males had a slightly higher age adjusted prevalence than females, although not statistically significant. Similar gender differences have been reported in other surveys (18).

Our analysis of incidence by age is hampered by our few cases, which forced us to limit the analysis to three age groups. Nevertheless the incidence rate in Ba Vi was higher in childhood compared with middle age, as in other studies, but not increased in oldest group which seems to be the rule in studies from developed countries (27, 29, 30, 80, 82). Our patter is, however, similar to other studies from developing countries (22, 37, 72, 73).

The prevalence rate in Ba Vi was highest among the young (age<10) and seemed to decline after the fifth decades. This pattern has been observed in other developing countries (22, 83, 84), while most of the studies from developed countries report an increase after 50 years of age (22, 83, 84).

We have no obvious explanation for the relatively low epilepsy prevalence among the elderly in our study although the age distribution in general is different in a developing country. In particular the number of elderly men in the population is small and our estimates thus less precise. One possibility is that elderly people, due to stigma, are less willing to disclose their epilepsy. Another possible contributing factor could be if elderly people with epilepsy in developing countries have a particularly high mortality rate.

An important advantage of our study is that we had access to data on socio-demographic conditions and could study their association with the incidence and prevalence of epilepsy. We found a significant association between living as single, low income, low education and high incidence of epilepsy. Similar observations have been made in the UK (85) and in Iceland (86). Single persons and those with low education also had a higher prevalence rate in our Ba Vi study. The causal direction of this association is unclear, but there is obviously a possibility of persons with epilepsy having less easy to find a partner and to get access to social networks, as indicated from our results in Paper I.

It is indeed intriguing that, with the exception of epilepsy among the elderly, our results on the incidence and prevalence rates of epilepsy and on their associations with socio-demographic conditions are very similar to what has been reported from Europe and North America. This is much in contrast with previous perceptions of the epidemiology of epilepsy in developing countries (19).

5.3 CLASSIFICATION OF SEIZURES AND EPILEPSY

The proportion of patients for whom we could make a more precise epilepsy classification was small. This is a reflection of the limitations inherent in a study from a rural region of a developing country. However, unlike most previous studies from other under-privileged regions most of our cases underwent an EEG examination and the majority of the incident cases also a CT-scan. The yield in terms of relevant pathology was low, however. It is likely that more cases would have been found to have epileptiform activity on EEG with an extended duration of the examination, and if photic stimulation would have been included. However, a low yield was also reported from Burundi, another developing country (87).

We were more surprised about the low yield of the CT-scans, only two out of 29 incident cases with significant abnormalities. It is very likely that some of the 11 cases who for various reasons did not participate would have had abnormalities on their scans. More importantly, however, none of our examined patients showed signs of neurocysticercosis. Obviously this is not a major cause of epilepsy in the Ba Vi district.

It should be stressed that also some recent studies from European countries have had difficulties in classifying incident cases with respect to specific type of epilepsy and underlying etiology despite access to EEG and neuroimaging (30, 81, 88).

5.4 TREATMENT GAP

We found a treatment gap of 84.7% (95% CI: 79.5% - 89.8%) among patients with active epilepsy in Ba Vi, which means that the large majority of persons with epilepsy are not on adequate treatment. This is higher than the mean of 64.3% in three Asian studies reported in a meta-analysis (89). The estimates, however, vary considerably between the three studied countries, being 98% in Pakistan (90), 38% in India (91) and 63% in China (35). A recent study from Tibet reported a treatment gap of 97% (92). This variation may reflect the type of the surveyed population as the treatment gap seems to be considerably higher in rural compared to urban regions (89). The district surveyed in our study is mainly rural, which thus could contribute to the high estimate. It should also be acknowledged that, like other researchers, we have not attempted to validate the patient's information concerning treatment.

In developing countries in sub-Saharan Africa and Latin America (93, 94), up to 90% of people with epilepsy receive inadequate treatment or no treatment at all. In Asian countries, the treatment gap was 29–98%, with values for most countries between 50% and 80%. The treatment gap was higher in rural areas than in urban areas.

The patients' explanations for not taking AEDs were informative. The major cause among those who never tried AEDs, as well as those who had discontinued treatment, was that they thought they had too few seizures to justify the drawbacks of treatment. The later included costs and time loss to obtain drugs. The very high treatment gap is remarkable considering the fact that the Vietnamese national programme for epilepsy is meant to include provision of some AEDs free of charge. Direct costs should therefore not be an issue. Patient's attitudes towards treatment indicate that they may be unaware of or underestimate the possible risks with seizures. It is also likely that the provided patient information on the nature of drug treatment for epilepsy has been insufficient.

5.5 KNOWLEDGE ATTITUDES AND PRACTICE TOWARD EPILEPSY

Personal and public knowledge about and attitudes toward epilepsy could have a major impact on the patients' willingness to disclose their condition, to maintain an appropriate drug treatment as well as on the epilepsy patients' everyday life in their community. We identified some significant differences between the results of our survey in the Ba Vi district in Vietnam and the results of similar surveys in other parts of the world. In particular, attitudes were more negative compared to most Western countries but also different from some Asian countries. Such differences are often considered to reflect national and cultural attitudes, but it cannot be excluded that cultural differences in willingness to disclose what might be considered a politically incorrect opinion could contribute.

Fewer in our study (67%) had heard or read about epilepsy compared to reports from Europe (95-99) the USA (100), New Zealand (101), South America (102), Ethiopia (103), and from most other countries in Asia (91, 104-110), although there are exceptions with similarly low

rates (106, 111). Differences were less obvious concerning the extent to which the respondents had known someone with epilepsy or had seen a seizure.

More than one third in our population objected to their children associating with someone with seizures, a proportion considerably higher than reported from Western (98-100, 112) and most Asian countries. Higher figures have only been found in surveys from some African countries (97, 103, 113, 114) and China (109). Even more of the respondents in Ba Vi, 82%, had objections to their children marrying someone with epilepsy. A similarly high percentage has only been reported from China (109) and Ethiopia (103). In surveys from Europe, the USA, New Zealand, and some Asian countries this proportion typically ranged from less than 10% up to some 30% (100, 102, 104, 112, 115-119).

Only one third of the respondents in Ba Vi thought that people with epilepsy could be employed in jobs like other people, fewer than in Western countries, and in Malaysia and Hong Kong where approximately 75 to 90% thought they should be (106, 110). Similarly low figures have, however, been reported from Taiwan (105), South Korea (104), Ethiopia (103) and even lower from Brazil (102).

Of our respondents 50% considered a brain lesion to be the main cause of epilepsy. This percentage was higher than those of surveys conducted in China in 1988 (25%) (109), Taiwan in 1992 (20%) (105), Myanmar in 2002 (33%) (108), and Malaysia in 1998 (11%) (91). Nevertheless, acceptance seemed to be poorer among the Vietnamese population.

Interestingly, Cuong and collaborators recently published a survey based on the same questionnaire applied to another population in Vietnam (111). That study was conducted in 2003 in the Nhan Chinh community in the peripheral region of Hanoi. Differences in the familiarity with epilepsy between the two studies were minor, but differences in attitudes were considerable, with those in Ba Vi in general being more negative. We were surprised to find that those among the Ba Vi respondents knowing someone with epilepsy were more likely to consider it a form of insanity. It is possible that psychiatric co-morbidity and a high prevalence of mental retardation among people with epilepsy could contribute to this association.

5.6 IMPLICATIONS FOR MANAGEMENT OF EPILEPSY IN VIETNAM

If our data were extrapolated to the entire Vietnamese population of 86 million inhabitants, one can estimate that there are approximately 378,000 persons in the country with active epilepsy requiring regular medical attention, and a large number of these without adequate treatment. Each year there are close to 38,000 new cases in need of diagnostic evaluation. Given the few trained neurologists in the country it is clear that the first level epilepsy care has to be provided by other health care professionals. It could, however, be the responsibility of the neurologists to set up and organise an efficient health care system to meet the needs of the many people with epilepsy.

Provided that our data on the treatment gap are representative, there are approximately 320,000 persons with active epilepsy in Vietnam that are without adequate treatment with AEDs and thus subject to the risks of uncontrolled epilepsy. This is remarkable considering the national programme which is meant to provide some major AEDs free of charge. The reasons expressed

by the patients who never tried AEDs were similar to those given by patients who had tried but stopped their treatment. The most common explanation was that patients considered treatment unnecessary. Other major reasons were that patients considered their epilepsy untreatable or high costs and unavailability of drugs. These observations have two major implications for the management of people with epilepsy. First, there is an obvious need for patient education. The patient responses reveal an underestimation of the risks associated with uncontrolled epilepsy but also of the possibilities for successful outcome with drug treatment. They need to be educated about this and about the nature of AED treatment. Second, there are obviously obstacles in the present model for provision of drug treatment. Although the AED may be free of charge, the indirect costs can be impossible to carry for the individual patient. As drugs are dispensed for only 10 days at a time, patients need to take frequent leaves from their work to refill their supplies. It is extremely important to improve the accessibility of AEDs, drugs that are meant to be used long term and were irregular intake can have drastic and sometimes even fatal consequences.

Finally, there is an urgent need to increase awareness and change the negative public attitudes toward epilepsy and people with epilepsy. The obvious method is public education. The aim should be reduction of the stigma associated with epilepsy and ultimately to allow people with epilepsy to live according to their full potentials.

6 CONCLUSIONS

- Knowledge of epilepsy among Vietnamese people is limited compared to some Western countries and the attitudes more negative.

- The prevalence of active epilepsy in Vietnam is similar to some other Asian countries but lower than in developing countries from Africa and South America. The risk of having epilepsy is related to socio-demographic conditions.

- 85% of people with active epilepsy in the present study were not on adequate treatment with AEDs despite a national programme providing some AEDs free of charge.

- The incidence rate of epilepsy in rural Vietnam in our study was lower than in developing countries in Latin America and Africa and similar to rates in Europe and North America. The association with socio-economic conditions was similar to the patterns reported from Europe and North America.

7 ACKNOWLEDGEMENTS

It is a pleasure to thank the many people who made this thesis possible.

First of all, I am heartily thankful to my supervisor, Professor Torbjörn Tomson, whose encouragement, guidance and support from the initial to the final level enabled me to develop an understanding of the subject. Throughout my thesis-writing period, he provided sound advice, good teaching, good company, and lots of good ideas, he helped to make "epilepsy research" fun for me. I would have been lost without him. He is the best supervisor I could ever have wished for.

I wish to express my warm and sincere thanks to my Vietnamese supervisor, Professor Le Quang Cuong, Head of the Department of Neurology, Hanoi Medical University, who introduced me to join the project and supported me during my time in Hanoi. His ideals and concepts have had a remarkable influence on my entire career in the field of epilepsy research.

I warmly thank my co-supervisor, Professor Peter Allebeck, for his effort in revising my manuscripts and thesis, for valuable advice and constructive criticism of this study.

I am grateful to Professor Nguyen Thi Kim Chuc for providing me with a great opportunity to work in Filabavi, for introducing me to the Filabavi Project and District hospital of Ba Vi for her generous support and arrangement from my beginning.

I owe my sincere gratitude to Hans E Persson MD., who gave me the opportunity to learn how to interpret the EEG in the Department of Clinical Neurophysiology and gave me untiring help during the survey.

My warm thanks are due to Associate Professor Ingeborg van de Ploeg for her enthusiasm in the common disease project, for your arrangement and support to me and all other Vietnamese students. Mrs. Monica Grangien, Mrs. Maissa Al-Adhami and Ms. Silsa Heilborn, for coordination and administration.

I wish to express my warm and sincere thanks to Professor Nguyen Lan Viet, Associate Professor Nguyen Duc Hinh at the Hanoi Medical University for accepting me as a PhD student in the common disease project, for your kindness, support and encouragement. Associate Professor Ta Thanh Van, PhD. Dang Thi Ngoc Dung, Mr. Nong Ngoc Huy, Mrs. Nguyen Thu Huong for administration and financial management.

I am indebted to the past or present members at the Department of Neurology, Hanoi Medical University for sharing scientific knowledge, providing time and creating extremely nice working atmosphere.

I wish to thank also the past or present members at the Department of Clinical Neuroscience, Karolinska Universitet in Solna for encouragement during my graduate study.

It is difficult to overstate my gratitude to Professor Le Van Thinh, Head of the Department of Neurology, Bach Mai Hospital, Professor Le Duc Hinh, former Head of the Department and all other colleagues for helping me and making this thesis possible.

This work would not have been possible without help from Filabavi Office of Filabavi Project in Ba Vi, Hanoi. I would like to thank Mrs. Minh, Long, Sang, other interviewers and field-

supervisors for helping with the interviews and recruitment of the patients and analyses of the data.

My deepest gratitude goes to my family for their unflagging love and support throughout my life. I am indebted to my parent Nguyen Van Tuong and Tran Thi Tan, for their care and love. They had never complained in spite of all the hardships in their life to support for my study. I cannot ask for more from them since they are simply perfect. I owe my loving thanks to my son Nguyen Minh Quan and my daughter Nguyen Thanh Thuy for their inspiration and joyfulness. They have lost a lot due to my research abroad. I feel proud of my sister, Bich, and her husband, Son, for their talents. Thank you for your love and constant support especially when I was in Sweden.
Lastly, I offer my regards and blessings to all of those who supported me in any respect during the completion of the project.

The study was supported by grants from Karolinska Institutet Research Training program (KIRT), the Swedish International Development Cooperation Agency, Sida/SAREC and the Karolinska University Hospital Research Funding.

Stockholm, April 13th, 2010
Nguyen Anh Tuan

8 REFERENCES

1. Eadie MJ, Bladin PF. A Disease Once Sacred: A History of the Medical Understanding of Epilepsy. Eastleigh: John Libbey; 2001.

2. Jankovic SM, Sokic DV, Levic ZM, Susic V, Stojsavljevic N, Drulovic J. [Epilepsy, eponyms and patron saints (history of Western civilization)]. Srp Arh Celok Lek. 1996 May-Jun;124(5-6):162-5.

3. Jackson J. Lectures on the diagnosis of epilepsy. Med Times Gazette. 1876;I.

4. Jung R, Berger W. [Fiftieth anniversary of Hans Berger's publication of the electroencephalogram. His first records in 1924--1931 (author's transl)]. Arch Psychiatr Nervenkr. 1979 Dec;227(4):279-300.

5. Tudor M, Tudor L, Tudor KI. [Hans Berger (1873-1941)--the history of electroencephalography]. Acta Med Croatica. 2005;59(4):307-13.

6. Jain S. Priority of epilepsy research in Asia. Epilepsia. 2005;46 Suppl 1:46-7.

7. Tseng WS. The development of psychiatric concepts in traditional Chinese medicine. Arch Gen Psychiatry. 1973 Oct;29(4):569-75.

8. Liu X. Psychiatry in traditional Chinese medicine. Br J Psychiatry. 1981 May;138:429-33.

9. Lee TM, Yang SH, Ng PK. Epilepsy in Chinese culture. Am J Chin Med. 2001;29(1):181-4.

10. Lai CW, Lai YH. History of epilepsy in Chinese traditional medicine. Epilepsia. 1991 May-Jun;32(3):299-302.

11. Huang-Di-Nei-Jing. Huang Di Nei Jing. Beijing: People's Health Publishing House; 1978.

12. Jacoby A, Wang W, Vu TD, Wu J, Snape D, Aydemir N, et al. Meanings of epilepsy in its sociocultural context and implications for stigma: findings from ethnographic studies in local communities in China and Vietnam. Epilepsy Behav. 2008 Feb;12(2):286-97.

13. Fisher RS, van Emde Boas W, Blume W, Elger C, Genton P, Lee P, et al. Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia. 2005 Apr;46(4):470-2.

14. Commission. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. Epilepsia. 1981;22:489-501.

15. Commission. Proposal for revised classification of epilepsies and epileptic syndromes. Commission on Classification and Terminology of the International League Against Epilepsy. Epilepsia. 1989 Jul-Aug;30(4):389-99.

16. Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde Boas W, et al. Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005-2009. Epilepsia. Feb 26.

17. Guidelines for epidemiologic studies on epilepsy. Commission on Epidemiology and Prognosis, International League Against Epilepsy. Epilepsia. 1993 Jul-Aug;34(4):592-6.

18. Banerjee PN, Filippi D, Allen Hauser W. The descriptive epidemiology of epilepsy-a review. Epilepsy Res. 2009 Jul;85(1):31-45.

19. Jallon P. Epilepsy in developing countries. Epilepsia. 1997;38:1143–51.

20. Commission. ILAE commission report, The Epidemiology of the Epilepsies: Future Directions. Epilepsia. 1997;38:614-8.

21. Meinardi H, Scott RA, Reis R, Sander JW. The treatment gap in epilepsy: the current situation and ways forward. Epilepsia. 2001 Jan;42(1):136-49.

22. Lavados J, Germain L, Morales A, Campero M, Lavados P. A descriptive study of epilepsy in the district of El Salvador, Chile, 1984-1988. Acta Neurol Scand. 1992 Apr;85(4):249-56.

23. Burneo JG, Tellez-Zenteno J, Wiebe S. Understanding the burden of epilepsy in Latin America: a systematic review of its prevalence and incidence. Epilepsy Res. 2005 Aug-Sep;66(1-3):63-74.

24. Brutto OHD, Santibanez R, Idrovo L. Epilepsy and Neurocysticercosis in Atahualpa: a door-to-door survey in rural coastal Ecuador. Epilepsia. 2005;46:583–7.

25. Placencia M, Shorvon SD, Paredes V, Bimos C, Sander JW, Suarez J, et al. Epileptic seizures in an Andean region of Ecuador. Incidence and prevalence and regional variation. Brain. 1992 Jun;115 (Pt 3):771-82.

26. Mac TL, Tran DS, Quet F, Odermatt P, Preux PM, Tan CT. Epidemiology, aetiology, and clinical management of epilepsy in Asia: a systematic review. Lancet Neurol. 2007 Jun;6(6):533-43.

27. Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984. Epilepsia. 1993 May-Jun;34(3):453-68.

28. Preux PM, Druet-Cabanac M. Epidemiology and aetiology of epilepsy in sub-Saharan Africa. Lancet Neurol. 2005 Jan;4(1):21-31.

29. Olafsson E, Hauser WA, Ludvigsson P, Gudmundsson G. Incidence of epilepsy in rural Iceland: a population-based study. Epilepsia. 1996 Oct;37(10):951-5.

30. Olafsson E, Ludvigsson P, Gudmundsson G, Hesdorffer D, Kjartansson O, Hauser WA. Incidence of unprovoked seizures and epilepsy in Iceland and assessment of the epilepsy syndrome classification: a prospective study. Lancet Neurol. 2005 Oct;4(10):627-34.

31. Forsgren L, Beghi E, Oun A, Sillanpaa M. The epidemiology of epilepsy in Europe - a systematic review. Eur J Neurol. 2005 Apr;12(4):245-53.

32. Carpio A, Hauser WA. Epilepsy in the developing world. Current Neurology & Neuroscience Reports. 2009;9(4):319-26.

33. Sander JW. Global Campaign Against Epilepsy. Overview of the demonstration projects. Epilepsia. 2002;43 Suppl 6:34-6.

34. WHO. Epilepsy management at a primary health level: protocol for a demonstration project in the People's Republic of China. WHO; 2000; Geneva; 2000.

35. Wang WZ, Wu JZ, Wang DS. The prevalence and treatment gap in epilepsy in China: an ILAE/IBE/WHO study. Neurology. 2003;60:1544–5.

36. Li SC, Schoenberg BS, Wang CC, Cheng XM, Zhou SS, Bolis CL. Epidemiology of epilepsy in urban areas of the People's Republic of China. Epilepsia. 1985 Sep-Oct;26(5):391-4.

37. Mani KS, Rangan G, Srinivas HV, Kalyanasundaram S, Narendran S, Reddy AK. The Yelandur study: a community-based approach to epilepsy in rural South India--epidemiological aspects. Seizure. 1998 Aug;7(4):281-8.

38. Wang W, Wu J, Wang D, Chen G, Wang T, Yuan C, et al. [Epidemiological survey on epilepsy among rural populations in five provinces in China]. Zhonghua Yi Xue Za Zhi. 2002 Apr 10;82(7):449-52.

39. Cuong LQ, Doanh NV, Jallon P. Prevalence of epilepsy in Thai Bao-Bac Ninh, a region in Vietnam affected by neurocysticercosis. Epilepsia. 2005;46:132.

40. Tomson T, Beghi E, Sundqvist A, Johannessen SI. Medical risks in epilepsy: a review with focus on physical injuries, mortality, traffic accidents and their prevention. Epilepsy Res. 2004 Jun;60(1):1-16.

41. Forsgren L, Hauser WA, Olafsson E, Sander JW, Sillanpaa M, Tomson T. Mortality of epilepsy in developed countries: a review. Epilepsia. 2005;46 Suppl 11:18-27.

42. Tomson T, Nashef L, Ryvlin P. Sudden unexpected death in epilepsy: current knowledge and future directions. Lancet Neurol. 2008 Nov;7(11):1021-31.

43. Ding D, Hong Z, Wang WZ, Wu JZ, de Boer HM, Prilipko L, et al. Assessing the disease burden due to epilepsy by disability adjusted life year in rural China. Epilepsia. 2006 Dec;47(12):2032-7.

44. Boonluksiri P. Risk of recurrence following a first unprovoked seizure in Thai children. Neurol J Southeast Asia. 2003;8:25–9.

45. Hauser WA, Rich SS, Lee JR, Annegers JF, Anderson VE. Risk of recurrent seizures after two unprovoked seizures. N Engl J Med. 1998 Feb 12;338(7):429-34.

46. Ben-Menachem E. Treatment of new onset seizures: predicting long-term outcome. Epilepsy Curr. 2006 Nov-Dec;6(6):184-5.

47. Mani KS, Rangan G, Srinivas HV. Epilepsy control with phenobarbital or phenytoin in rural south India: the Yelandur study. Lancet. 2001;357:1316–20.

48. Wang WZ, Wu JZ, Ma GY. Efficacy assessment of phenobarbital in epilepsy: a large community-based intervention trial in rural China. Lancet Neurol. 2006;5:46–52.

49. Randomised study of antiepileptic drug withdrawal in patients in remission. Medical Research Council Antiepileptic Drug Withdrawal Study Group. Lancet. 1991 May 18;337(8751):1175-80.

50. Lossius MI, Hessen E, Mowinckel P, Stavem K, Erikssen J, Gulbrandsen P, et al. Consequences of antiepileptic drug withdrawal: a randomized, double-blind study (Akershus Study). Epilepsia. 2008 Mar;49(3):455-63.

51. Glauser T, Ben-Menachem E, Bourgeois B, Cnaan A, Chadwick D, Guerreiro C, et al. ILAE treatment guidelines: evidence-based analysis of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. Epilepsia. 2006 Jul;47(7):1094-120.

52. Fisher RS, Vickrey BG, Gibson P, Hermann B, Penovich P, Scherer A, et al. The impact of epilepsy from the patient's perspective II: views about therapy and health care. Epilepsy Res. 2000 Aug;41(1):53-61.

53. Marson AG, Al-Kharusi AM, Alwaidh M, Appleton R, Baker GA, Chadwick DW, et al. The SANAD study of effectiveness of valproate, lamotrigine, or topiramate for generalised and unclassifiable epilepsy: an unblinded randomised controlled trial. Lancet. 2007 Mar 24;369(9566):1016-26.

54. Marson AG, Al-Kharusi AM, Alwaidh M, Appleton R, Baker GA, Chadwick DW, et al. The SANAD study of effectiveness of carbamazepine, gabapentin, lamotrigine, oxcarbazepine, or topiramate for treatment of partial epilepsy: an unblinded randomised controlled trial. Lancet. 2007 Mar 24;369(9566):1000-15.

55. Zhang TM. Dianxian Zhiliao Lingyan Fang (Effective prescriptions for treating epilepsy). Beijing: People; 1996.

56. Wang T. Effects of Chinese medicine zhenxianling in 239 cases of epilepsy. J Tradit Chin Med. 1996 Jun;16(2):94-7.

57. Mac TL, Le VT, Vu AN. AEDs availability and professional practice in delivery outlets in a city centre in southern Vietnam. Epilepsia. 2006;47:330–4.

58. Mac TL, Gaulier JM, Le VT, Vu AN, Preux PM, Ratsimbazafy V. Quality of antiepileptic drugs in Vietnam. Epilepsy Res. 2008 Jul;80(1):77-82.

59. Gellert GA. The influence of market economics on primary health care in Vietnam. Jama. 1995 May 17;273(19):1498-502.

60. Knowles J. Some key health insurance policy issues in Viet Nam. Hanoi: Asian Development Bank.; 2007.

61. Ensor T. Introducing health insurance in Vietnam. Health Policy Plan. 1995 Jun;10(2):154-63.

62. Tuan T, Dung VT, Neu I, Dibley MJ. Comparative quality of private and public health services in rural Vietnam. Health Policy Plan. 2005 Sep;20(5):319-27.

63. Lim SH, Tan CT. Training and certification of neurologists in South East Asia. Neurology Asia. 2007;12:47-52.

64. Chuc NT, Diwan V. FilaBavi, a demographic surveillance site, an epidemiological field laboratory in Vietnam. Scandinavian Journal of Primary Health Care Supplement 2003;62:3-7.

65. Byass P. Patterns of mortality in Bavi, Vietnam, 1999-2001. Scand J Public Health Suppl. 2003;62:8-11.

66. Beghi E, Carpio A, Forsgren L, Hesdorffer DC, Malmgren K, Sander JW, et al. Recommendation for a definition of acute symptomatic seizure. Epilepsia. 2009 Sep 3.

67. Ahmad O, Boschi-Pinto C, Lopez A, Murray C, Lozano R, Inoue M. Age standardization of rates: a new WHO standard. In GPE Discussion Paper

Series: no31. World Health Organization. 2000.

68. Quet F, Odermatt P, Preux PM. Challenges of epidemiological research on epilepsy in resource-poor countries. Neuroepidemiology. 2008;30(1):3-5.

69. Sander JW. The epidemiology of epilepsy revisited. Curr Opin Neurol. 2003 Apr;16(2):165-70.

70. MacDonald BK, Cockerell OC, Sander JW, Shorvon SD. The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. Brain. 2000 Apr;123 (Pt 4):665-76.

71. Benn EK, Hauser WA, Shih T, Leary L, Bagiella E, Dayan P, et al. Estimating the incidence of first unprovoked seizure and newly diagnosed epilepsy in the low-income urban community of Northern Manhattan, New York City. Epilepsia. 2008 Aug;49(8):1431-9.

72. Rwiza HT, Kilonzo GP, Haule J, Matuja WB, Mteza I, Mbena P, et al. Prevalence and incidence of epilepsy in Ulanga, a rural Tanzanian district: a community-based study. Epilepsia. 1992 Nov-Dec;33(6):1051-6.

73. Tekle-Haimanot R, Forsgren L, Ekstedt J. Incidence of epilepsy in rural central Ethiopia. Epilepsia. 1997 May;38(5):541-6.

74. Koul R, Razdan S, Motta A. Prevalence and pattern of epilepsy (Lath/Mirgi/Laran) in rural Kashmir, India. Epilepsia. 1988;29:116–22.

75. Osuntokun BO, Adeuja AO, Nottidge VA, Bademosi O, Olumide A, Ige O, et al. Prevalence of the epilepsies in Nigerian Africans: a community-based study. Epilepsia. 1987 May-Jun;28(3):272-9.

76. Annegers JF, Hauser WA, Lee JR, Rocca WA. Incidence of acute symptomatic seizures in Rochester, Minnesota, 1935-1984. Epilepsia. 1995 Apr;36(4):327-33.

77. Jallon P, Goumaz M, Haenggeli C, Morabia A. Incidence of first epileptic seizures in the canton of Geneva, Switzerland. Epilepsia. 1997 May;38(5):547-52.

78. Jallon P, Smadja D, Cabre P, Le Mab G, Bazin M. EPIMART: prospective incidence study of epileptic seizures in newly referred patients in a French Carribean island (Martinique). Epilepsia. 1999 Aug;40(8):1103-9.

79. Keranen T, Riekkinen PJ, Sillanpaa M. Incidence and prevalence of epilepsy in adults in eastern Finland. Epilepsia. 1989 Jul-Aug;30(4):413-21.

80. Forsgren L, Bucht G, Eriksson S, Bergmark L. Incidence and clinical characterization of unprovoked seizures in adults: a prospective population-based study. Epilepsia. 1996 Mar;37(3):224-9.

81. Adelow C, Andell E, Amark P, Andersson T, Hellebro E, Ahlbom A, et al. Newly diagnosed single unprovoked seizures and epilepsy in Stockholm, Sweden: First report from the Stockholm Incidence Registry of Epilepsy (SIRE). Epilepsia. 2009 May;50(5):1094-101.

82. Sidenvall R, Forsgren L, Blomquist HK, Heijbel J. A community-based prospective incidence study of epileptic seizures in children. Acta Paediatr. 1993 Jan;82(1):60-5.

83. Basch EM, Cruz ME, Tapia D, Cruz A. Prevalence of Epilepsy in a Migrant Population near Quito, Ecuador. Neuroepidemiology. 1997;16:94-8.

84. Birbeck GL, Kalichi EM. Epilepsy prevalence in rural Zambia: a door-to-door survey. Trop Med Int Health. 2004 Jan;9(1):92-5.

85. Heaney DC, MacDonald BK, Everitt A, Stevenson S, Leonardi GS, Wilkinson P, et al. Socioeconomic variation in incidence of epilepsy: prospective community based study in south east England. Bmj. 2002 Nov 2;325(7371):1013-6.

86. Hesdorffer DC, Tian H, Anand K, Hauser WA, Ludvigsson P, Olafsson E, et al. Socioeconomic status is a risk factor for epilepsy in Icelandic adults but not in children. Epilepsia. 2005 Aug;46(8):1297-303.

87. Diagana M, Nsengiyumva G, Tuillas M, Druet-Cabanac M, Bouteille B, Preux PM, et al. Electroencephalograms (EEG) in 250 patients with epilepsy in a cysticercosis endemic area in Burundi. Neurophysiol Clin. 2005;35(1):1-10.

88. Annegers JF, Dubinsky S, Coan SP, Newmark ME, Roht L. The incidence of epilepsy and unprovoked seizures in multiethnic, urban health maintenance organizations. Epilepsia. 1999 Apr;40(4):502-6.

89. Mbuba CK, Ngugi AK, Newton CR, Carter JA. The epilepsy treatment gap in developing countries: a systematic review of the magnitude, causes, and intervention strategies. Epilepsia. 2008 Sep;49(9):1491-503.

90. Aziz H, Guvener A, Akhtar S. Comparative epidemiology of epilepsy in Pakistan and Turkey: population based studies using identical protocols. Epilepsia. 1997;38:716–22.

91. Radhakrishnan K, Pandian JD, Santhoshkumar T, Thomas SV, Deetha TD, Sarma PS, et al. Prevalence, knowledge, attitude, and practice of epilepsy in Kerala, South India. Epilepsia. 2000;41(8):1027-35.

92. Zhao Y, Zhang Q, Tsering T, Sangwan, Hu X, Liu L, et al. Prevalence of convulsive epilepsy and health-related quality of life of the population with convulsive epilepsy in rural areas of Tibet Autonomous Region in China: an initial survey. Epilepsy Behav. 2008 Apr;12(3):373-81.

93. Shorvon SD, Farmer P. Epilepsy in developing countries: a review of epidemiological, sociocultural and treatment aspects. Epilepsia. 1988;29 (suppl 1):S36–S45.

94. Scott RA, Lhatoo SD, Sander J. The treatment of epilepsy in developing countries: where do we go from here? Bull World Health Organ. 2001;79:344–51.

95. Jensen R, Dam M. Public attitudes toward epilepsy in Denmark. Epilepsia. 1992;33(3):459-63.

96. Novotná, Rektor I. The trend in public attitudes in the Czech Republic towards persons with epilepsy. European Journal of Neurology. 2002;9:535-40.

97. Nubukpo P, Preux PM, Clement JP, Houinato D, Tuillas M, Aubreton C, et al. Comparison of sociocultural attitudes towards epilepsy in Limousin (France), in Togo and in Benin (Africa). Medecine Tropicale (Marseilles). 2003;63(2):143-50.

98. Spatt J, Bauer G, Baumgartner C, Feucht M, Graf M, Mamoli B, et al. Predictors for negative attitudes toward subjects with epilepsy: a representative survey in the general public in Austria. Epilepsia. 2005 May 2006;46(5):736-42.

99. Mirnics Z, Czikora G, Zavecz T, Halasz P. Changes in public attitudes toward epilepsy in Hungary: results of surveys conducted in 1994 and 2000. Epilepsia. 2001 Jan;42(1):86-93.

100. Kobau R, Price P. Knowledge of epilepsy and familiarity with this disorder in the U.S. population: results from the 2002 HealthStyles Survey. Epilepsia. 2003;44(11):1449-54.

101. Hills, MacKenzie HC. New Zealand community attitude toward people with epilepsy. Epilepsia. 2002;43:1583-9.

102. Santos IC, Guerreiro MM, Mata A, Guimaraes R, Fernandes L, Moreira Filho DC, et al. Public awareness and attitudes toward epilepsy in different social segments in Brazil. Arquivos de Neuro-Psiuiatria. 1998;56(1):32-8.

103. Tekle Haimanot R, Abebe M, Forsqren L, Gebre Mariam A. Attitudes of rural people in central Ethiopia towards epilepsy. Social science & medicine. 1991;32(2):203-9.

104. Choi-Kwon S, Park KA, Lee HJ, Park MS, Lee CH, Cheon SE, et al. Familiarity with, knowledge of, and attitudes toward epilepsy in residents of Seoul, South Korea. Acta Neurologica Scandinavica. 2004;110(1):39-45.

105. Chung MY, Chang YC, Lai YHC. Survey of public awareness, understanding and attitudes toward epilepsy in Taiwan. Epilepsia. 1995;36:488-93.

106. Fong CY, Hung A. Public awareness, attitude, and understanding of epilepsy in Hong Kong Special Administrative Region, China. Epilepsia. 2002 2002 Mar;43(3):311-6.

107. Kim MK, Kim IK, Kim BC, Cho KH, Kim SJ, JD. M. Positive trends of public attitudes toward epilepsy after public education campaign among rural korean residents. Journal of Korean Medical Science. 2003;18(2):248-54.

108. Win NN, Chit Soe. Public awareness, attitude and understanding toward epilepsy among Myanmar people. Neurological Journal of South East Asia. 2002;7:81-8.

109. Lai CW, Huang XS, Lai YHC. Survey of public awareness, understanding and attitudes toward epilepsy in Henan province, China. Epilepsia. 1990;31:182-7.

110. Ramamasundrum V, Mohd Hussin ZA, Tan CT. Public awareness, attitude and understanding towards epilepsy in Kelantan, Malaysia. Neurological Journal of South East Asia. 2000;5:55–60.

111. Cuong LQ, Thien DD, Jallon D. Survey of public awareness, attitudes, and understanding toward epilepsy in Nhan Chinh, Hanoi, Vietnam, in 2003. Epilepsy & Behavior 2006 February 2006;8(1):176-80.

112. Andriantseheno LM, Rakotoarivony MC. Sociocultural aspects of epilepsy in Madagascar. K.A.P. survey carried out in Antananarivo. Bulletin de la Societe de Pathologie Exotique. 2000;93(4):247-50.

113. Atadzhanov M, Chomba E, Haworth A, Mbewe E, Birbeck GL. Knowledge, attitudes, behaviors, and practices regarding epilepsy among Zambian clerics. Epilepsy & Behavior. 2006;9(1):83-8.

114. El Sharkawy G, Newton C, Hartley S. Attitudes and practices of families and health care personnel toward children with epilepsy in Kilifi, Kenya. Epilepsy & Behavior. 2006;8(1):201-12.

115. Bener A, al-Marzooqi FH, Sztriha L. Public awareness and attitudes towards epilepsy in the United Arab Emirates. Seizure. 1998;7(3):219-22.

116. Dawkins JL, Crawford PM, Stammers TG. Epilepsy: a general practice study of knowledge and attitudes among sufferers and non-sufferers. British Journal of General Practice. 1993;43(376):453-7.

117. Gambhir SK, Kumar V, Singhi PD, Goel RC. Public awareness, understanding & attitudes toward epilepsy. Indian Journal of Medical Research. 1995;102:34-8.

118. Seneviratne U, Rajapakse P, Pathirana R, Seetha T. Knowledge, attitude, and practice of epilepsy in rural Sri Lanka. Seizure. 2002;11(1):40-3.

119. Tan CT, Lim SH. Epilepsy in South East Asia. Neurological Journal of South East Asia. 1997;2:11-5.