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The prevalence and treatment gap of epilepsy in Tbilisi, Georgia

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Summary
Introduction: Data on the prevalence of epilepsy and the extent of its treatment gap are important for planning health care delivery for people with epilepsy. The prevalence of active epilepsy in Georgia prior to the social and political re-organization in the early 1990s was estimated at around 5.7 per 1000. Changes to the social structure of the country may have affected this. There is no previous estimate of the treatment gap.
Methods: A door-to-door survey was carried out using a validated screening questionnaire to determine the prevalence of epilepsy and the extent of the treatment gap amongst a population of about 10,000 people in Tbilisi, the capital of Georgia. The diagnosis of epilepsy amongst those who screened positive was confirmed by a multidisciplinary team.
Results: Lifetime prevalence was 11.4/1000. The prevalence of active epilepsy was estimated at 8.8/1000, and 5/1000 had seizures in the previous 12 months. About two thirds of people with active epilepsy had not received appropriate antiepileptic treatment in the month prior to the survey. 89% had focal epilepsy and two thirds had co-morbidity (neurological deficits, behavioral, psychiatric or somatic problems).
Conclusion: The prevalence of epilepsy was higher than previously estimated and the treatment gap was substantial. Results should inform the planning of epilepsy care delivery in the country.

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Introduction

Epilepsy is one of the most common chronic neurological conditions, affecting over 50 million people worldwide (Bell and Sander, 2001; Sander, 2003; Ngugi et al., 2010). It is a particular problem in low income countries, where significant numbers of people with epilepsy do not receive appropriate treatment. The ILAE/IBE/WHO Global Campaign against Epilepsy (GCAE) was established in order to ameliorate this problem. One of the goals of the GCAE was the introduction and assessment of measures which can lead to the reduction of the treatment gap (European Concerted Action and Research in Epilepsy, 2001).

Georgia is one of the republics of the former Soviet Union, with a population of 4,390,000 people, of whom up to 1,500,000 live in Tbilisi (Ministry of Labor, Health and Social Affairs, 2008). Social and political reorganization as a result of the break up of the former Soviet Union caused upheaval in the health system. An epidemiological study conducted prior to the reforms found the prevalence of active epilepsy to be 5.7/1000 (Geladze et al., 1995), and it was estimated that there were 25,000—30,000 people with active epilepsy in Georgia at the time. As a result of the social reorganization the country went into an economic crisis and it is probable that this led to an increase in the number of people with chronic conditions who were not treated appropriately (Tatishvili, 1997). In parallel, a return to traditional forms of medicine was seen and the use of alternative treatment also increased (Djibuti and Shakarishvili, 2003).

We carried out a study to ascertain the prevalence of epilepsy and to estimate its treatment gap, to inform the planning of epilepsy care delivery in the country. The study was carried out under the auspices of the ILAE/IBE/WHO ''Demonstration Project on Epilepsy in Georgia'' and the Georgian State Program ''Prevention and Diagnosis of Epilepsy''.

Methods

Definitions

The following definitions and criteria (Commission on Epidemiology and Prognosis, 1993; ILAE Commission Report, 1997) were used in the study:

Person with active epilepsy: a person with epilepsy who had had at least one epileptic seizure in the previous 5 years, regardless of antiepileptic drug treatment status. In addition, a more pragmatic clinical definition of active epilepsy and which instructed treatment was also used: an individual who had had unprovoked epileptic seizures which were disabling to the person on at least two different days in the previous 12 months.

Prevalence of active epilepsy: the number of people with active epilepsy in a given population at a specific time per thousand population.

Lifetime prevalence: the number of people who had ever had a seizure in a given population at a specific time per thousand population.

Appropriate treatment: diagnosis and treatment of underlying causes and treatment of recurrent seizures according to international standards.

Untreated epilepsy: any person with active epilepsy, who did not receive appropriate anti-epileptic drug (AED) treatment in the one month preceding identification.

Treatment gap: the difference between the number of people with active epilepsy and the number whose seizures were being appropriately treated in a given population at a given point of time, expressed as a percentage. This definition included both diagnostic and therapeutic deficits.

Seizures, epilepsies and epilepsy syndromes were classified according to the ILAE classifications for seizures (Commission of Classification and Terminology, 1981) and syndromes (Commission on Classification and Terminology, 1989).

Drug dose was based on national guidelines (National Clinical Practice Guideline, 2007). AED doses below those recommended for particular drugs were considered inadequate.

Study area, population and sampling procedures

The survey was conducted between June and November 2008 in seven districts of Tbilisi: Gldani, Nadzaladevi, Didube, Chugureti, Isani, Samgori and Saburtalo with an estimated population of 762,500. Cluster sampling was used to delineate the sampling frame. All people in the target household were interviewed. In cases of refusal, the neighboring dwelling was approached. The final study sample consisted of about 10,000 people and the prevalence of epilepsy and of the treatment gap were estimated based on the findings in these people.

Participant flow and diagnostic procedures

A screening questionnaire based on one used previously in China (Wang et al., 2003) was used. The questionnaire was adapted and subjected to Georgian-English onward-backward translation before the final version was validated (Placencia et al., 1992). This validation process was carried out at the Epilepsy Centre of the Institute of Neurology and Neuropsychology (INN) and showed sensitivity 98.8% and specificity 87.0%.

Ten general practitioners who had previously shown an interest in epilepsy were selected according to established criteria (previous experience of similar activity in the past, good interpersonal relations, and potential catchment of at least 2500 people). These personnel had the same level of epilepsy training and knowledge as general practitioners at other Primary Health Care (PHC) settings. They were trained in standardized techniques and approaches to ensure accurate completion of questionnaires and adherence to ethical guidelines. A door-to-door survey was used, and people were asked to complete the questionnaire after informed consent was received from the respondents. A questionnaire was completed for each individual based on his/her own replies; for small children, or people with intellectual disabilities, however, the questionnaires were completed based on responses from their mothers or guardians. After questionnaire completion, a neurologist with training in epilepsy reviewed each person who screened positive at the local PHC facility. This review consisted of an interview and a neurological examination. Those identified as possible cases were then reviewed further by a qualified epileptologist, had an MRI brain scan, neuropsychological assessment and an EEG at the Epilepsy Centre.

For the interictal EEG, a 16-channel system was used (standard 10—20 system of electrode placement (Jasper, 1958) with

longitudinal bipolar montage). Recording time averaged 20 min. Background activity was recorded 3 min before and after enhancing maneuvers (eyes open and closed, photo-stimulation at 3, 6, 10, 14, 20, 24 Hz, and hyperventilation).

Brain MR scanning was carried out on a 1.5 T Siemens Magnetom Avanto scanner. Sequences using the following protocols were obtained: T2 (tse)—axial plane; FLAIR—axial and coronal planes; (PD + T9tse)—coronal plane; T1 (MPRAGE) — 1 mm — coronal plane.

Statistical analysis

Descriptive statistics were used for categorical variables. Age- and sex-specific prevalence rates with 95% confidence intervals (CIs) were calculated for active epilepsy (Kirkwood and Sterne, 2003). Statistical analyses were performed in SPSS (version 16.0).

Ethics approval

The National Council on Bioethics scrutinized the protocol for the intervention and provided ethics approval.

Results

Less than 1% of respondents of the initial sampling frame were not interviewed for various reasons. In addition, a further 26 houses appeared to be unoccupied. A total of 10,326 people were interviewed, of whom 10,042 were considered to be valid responders (284 questionnaires were invalid, because of incomplete data). Nineteen percent (1859 people) screened positive and were identified as possible cases. After a neurological review, 499 people (5%) were identified as possibly having seizures. After specialist review at the Centre, the diagnosis of epilepsy was ruled out in 384 people. Of these, 41 had a single epileptic seizure and 126 had acute symptomatic seizures. The remaining 217 people had an alternative diagnosis including dissociative seizures.

The diagnosis of epilepsy was confirmed in 115 people (lifetime prevalence 11 per 1000, 95% CI 9.5—13.7), of whom 27 were seizure free; AEDs had been withdrawn in 16 of these and 11 were on AED therapy but had been seizure free for more than 5 years. The remaining 88 people had active epilepsy (i.e. had experienced at least one epileptic seizure in the last five years). Eight of these were prescribed AEDs, but had stopped on their own volition, 66 were on treatment. Fourteen people were newly diagnosed as having epilepsy during the study, of whom 12 had had seizures for more than one year (Table 1). For more details of participant flow, see Fig. 1.

Prevalent cases of epilepsy

The prevalence of active epilepsy, defined as having had at least one epileptic seizure in the previous five years, was 8.8 per 1000 (95% CI 7.1—10.8). Fifty-five percent ($n = 48$) were females; gender specific prevalence rates were 9.3 per thousand for men and 8.4 per 1000 for women (Table 2). The prevalence was generally, but not always, higher in males than in females, but neither the overall difference nor any age specific differences were statistically significant. The overall age specific prevalence was relatively constant in people in the age groups of 21 years old and above. Forty-nine people met the criteria for the pragmatic treatment definition, i.e. had had two or more seizures in the previous 12 months; the prevalence according to this definition was 5.0/1000 (CI 95% 3.7—6.5).

Appropriate treatment and the treatment gap

Twenty-five (34%) of the 74 people on prescribed AEDs and with previously diagnosed epilepsy were appropriately treated in the 4 weeks prior to the survey. The remaining 49 were either taking an AED not appropriate for their epilepsy syndrome or were using sub-therapeutic doses (or had stopped altogether [$N = 8$]). The treatment gap was estimated at 66%. Fourteen people had their first diagnosis of epilepsy made during the study. Of these, two had a recent onset of seizures. The remaining twelve people had had seizures for longer than one year. These could be considered as having failure of diagnosis and if they were included in the estimation of the treatment gap it would increase to 71% (Table 3).

Seizure types and etiological factors

Seizure types were classified in 86 (98%) people with active epilepsy and they could not be classified in the remaining two people. Seventy-seven (88%) people were classified as having partial seizures (PS) and most were symptomatic or cryptogenic. Nine (10%) were classified as having generalized seizures (GS) (Table 4).

Magnetic resonance imaging findings

MRI scans were obtained in 86 of the 88 people with active epilepsy. Two with intellectual disabilities were not investigated. In 56% of people the scan was reported as normal. The most common abnormalities seen were: cortical atrophy (16%), cerebro-vascular lesion (6%) and posttraumatic (5%) or postoperative (meningioma) cyst (1%). In one, relapse of a meningioma was seen. For more details see Table 5.

EEG

Interictal EEG was performed in all 88 people with epilepsy: in 33 (38%) no interictal abnormalities were recorded. Of the remaining 55 people, in 26 (30%) specific interictal epileptiform EEG abnormalities were seen (i.e. spike, spike wave, poly-spike, poly-spike waves, grouped sharp waves), and in 29 (33%) people focal abnormalities without specific epileptiform phenomena were observed. In one person a partial seizure occurred at the time of EEG recording. For more details see Table 6.

Co-morbidities

Neurological and psychiatric disabilities associated with seizures were sought for people with active epilepsy. One third ($n = 32$) had only epilepsy. Intellectual disability was found in 31 (35%) people, behavioral problems in 37 (42%), neurological deficits were identified in 11 (12.5%) people and 14 (16%) had psychiatric problems.

Table 1 Details of individuals with epilepsy for more than one year, newly diagnosed during the study.

Syndrome	*N*	Notes
Juvenile absence epilepsy	1	Duration 2 years. Absences with one episode of generalized tonic–clonic seizure. Characteristic EEG changes
Juvenile myoclonic epilepsy	1	Duration 1.5 years. Myoclonus only
Rolandic epilepsy	1	Duration 4 years. Characteristic EEG changes
Cryptogenic (4) and symptomatic (5) focal epilepsy	9	Median duration 7 years (range 3–22 years). Five had infrequent secondary generalization.

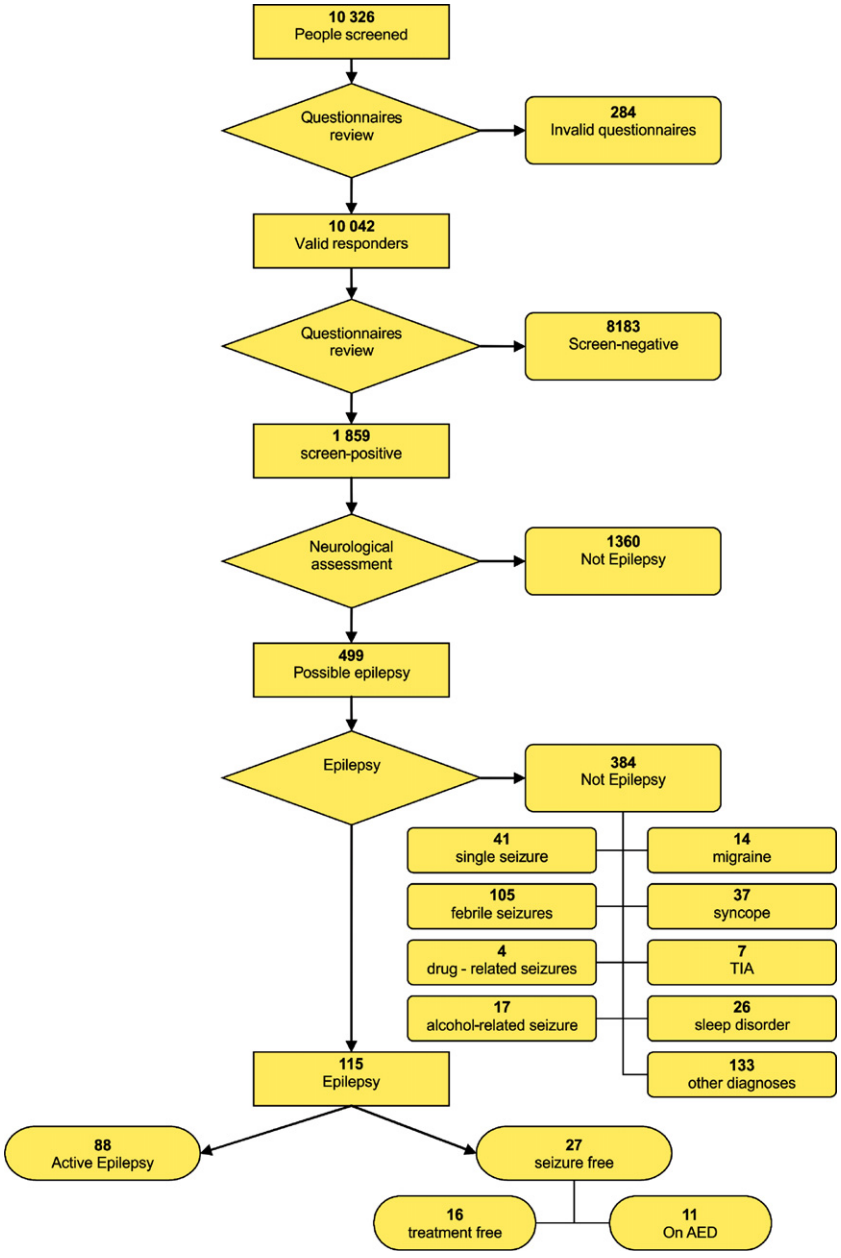

Figure 1 Participant flow chart.

Table 2 Age- and sex-specific prevalence of epilepsy in Tbilisi (per 1000 people).

Age (years)	Male				Female				Total			
	Population (thousands)	Cases	Rate	95% CI	Population (thousands)	Cases	Rate	95% CI	Population (thousands)	Cases	Rate	95% CI
0–5	318	2	6.3	1.6, 25.1	308	0	N/A		626	2	3.2	0.8, 12.8
6–10	415	4	9.6	3.6, 25.7	323	2	6.2	1.5, 24.8	738	6	8.1	3.7, 18.1
11–20	698	8	11.5	5.7, 22.9	764	13	17.0	9.9, 29.3	1462	21	14.4	9.4, 22.0
21–40	1311	10	7.6	4.1, 14.2	2005	17	8.5	5.3, 13.6	3316	27	8.1	5.6, 11.9
41–60	1036	9	8.7	4.5, 16.7	1516	12	7.9	4.5, 13.9	2552	21	8.2	5.4, 12.6
61+	518	7	13.5	6.4, 28.3	830	4	4.8	1.8, 12.8	1348	11	8.2	4.5, 11.7
Total	4296	40	9.3	6.8, 12.7	5746	48	8.4	6.3, 11.1	10,042	88	8.8	7.1, 10.8

Discussion

Epilepsy is associated with considerable physical and psychological morbidity causing a heavy burden for health systems, especially in resource-poor settings where the majority of people with epilepsy live. In the 1980s the first epidemiological studies in Georgia suggested that the prevalence of active epilepsy (having at least one seizure in the previous five years, regardless of AED treatment status) varied from 5 to 12/1000 in different regions of the country (mean prevalence 5.7/1000) (Geladze et al., 1995).

In the 1990s, Georgia faced an economic crisis and its economy plummeted. After regaining its independence, one third of the territory of Georgia went out of its area of jurisdiction; as a result, up to 500,000 refugees have been living in poor social economic conditions in various parts of the country. Health care reforms began but in many conditions, particularly chronic ones such as epilepsy, they were unsuccessful. In 1997 epilepsy was removed from the Georgian health care system. Such dramatic changes must have a negative impact on the epidemiology and treatment of epilepsy.

This study provides new epidemiological data for epilepsy in Tbilisi, where up to a third of the Georgian population lives. The prevalence is higher than previously reported (8.8 per 1000 people). It is estimated that up to 50,000 people with active epilepsy require long-term AED treatment and health management.

Using the more pragmatic definition (i.e. an individual who had had unprovoked epileptic seizures which were disabling to the person on two or more different days in the previous 12 months), the prevalence of active epilepsy is similar (5 per 1000) to published epidemiological data from other countries (Oun et al., 2003).

The poor socio-economic conditions in Georgia and the difficult situation in past years may well be responsible for worsening the situation regarding epilepsy care. The lifetime prevalence of epilepsy or the number of people who had ever had a non-febrile seizure (Cockerell et al., 1995), was higher in Georgia (11 per 1000) than in other Asian Countries (7 per 1000 in China; 9.98 per 1000 in Pakistan; 7.5 per 1000 in Turkey) (Aziz et al., 1997).

There were difficulties in the process of identifying people with a history of epilepsy and thus in calculating lifetime prevalence. The major cause may be stigma, which is strongly associated with epilepsy. Due to the high level of stigma, of 27 people with successful treatment of epilepsy, 24 people (13 who had had AEDs withdrawn and 11 who were seizure free but still took AEDs) had problems accepting that they had had seizures or had taken AEDs.

It is of interest that a high proportion of people in the study had partial forms of epilepsy. Almost 90% had either EEG, imaging or clinical evidence of partial onset. This is one of the highest rates identified in epidemiological surveys. It is possible that this was due to the methodology used; it is likely that the comprehensive investigation package received during case ascertainment is responsible for these findings. This will need further investigation. In one patient re-growth of a meningioma was shown by the MRI scan.

Table 3 Two calculations of percentage of people with active epilepsy with appropriate treatment.

Treatment	Those with previous diagnosis of epilepsy (*N* = 74)	Including those with new diagnosis of epilepsy, but duration >1 year (*N* = 86)
Correct treatment	25 (34%)	25 (29%)
Correct AED with sub-therapeutic dosage	29 (39%)	29 (34%)
AED not appropriate for epilepsy syndrome	12 (16%)	12 (14%)
Changed or stopped by the individual	8 (11%)	8 (9%)
Diagnostic failure	—	12 (14%)
Overall incorrect	49 (66%)	61 (71%)

Table 4 Percentage of seizure types and etiological factors.

	N (%)
Seizure types	
Partial seizures	77 (88)
Partial only	18 (21)
Partial with secondary generalized seizures	44 (50)
Nocturnal secondary generalized tonic—clonic seizures	15 (17)
Primary generalized	9 (10)
Unclassifiable	2 (2)
Etiological factors	
Symptomatic	40 (46)
Cryptogenic	37 (42)
Idiopathic	11 (13)
Partial	2 (2)
Generalized	9 (10)

Table 5 MR imaging findings amongst 86 patients with active epilepsy.

MRI findings	*N* (%)
Cortical atrophy	14 (16)
Cyst (posttraumatic-4, postoperative-1)	5 (6)
Cortical malformations	5 (6)
Post-stroke (ischemic/hemorrhagic) lesion	4 (4)
AVM	2 (2)
Lacunar infarction	2 (2)
Mesiotemporal sclerosis/atrophy	2 (2)
Repeat growth of meningioma	1 (1)
Cavernoma	1 (1)
Demyelinating lesions	1 (1)
Tuberous sclerosis	1 (1)
Normal	48 (56)

AVM: arterio—venous malformation.

Table 6 EEG findings in 88 patients with active epilepsy.

EEG patterns	*N* (%)
Generalized epilepsy	
No interictal activities	4 (5)
Specific interictal activities	2 (2)
Non specific interictal phenomena	3 (3)
Focal epilepsy	
No interictal activities	29 (33)
Specific interictal activities	24 (27)
Non specific interictal phenomena	26 (30)

Two different approaches were used to estimate the treatment gap. Initially it was calculated amongst 74 people with an established diagnosis of epilepsy. Only 25 were taking appropriate AED therapy, thus the treatment gap was 66%. If, however, the 12 people who had had undiagnosed epilepsy for more than a year were included in the calculations as having inadequate treatment, then the treatment gap rises to 71%.

High social and financial burdens affect people with improperly treated epilepsy and their families. Causes of inadequate treatment vary between countries and may be related to cultural and ethnic differences (Meinardi et al., 2001; Tovuudorj, 2007; Scott et al., 2001). Erroneous beliefs and low public awareness may persuade people with epilepsy and their families to hide the condition and cause inadequate health-seeking behavior.

Another problem may be the costs of AEDs which are paid 'out of pocket' in Georgia. According to the 2005 State Census, 16% of the overall population of Georgia and more than 50—60% of people with epilepsy are socially disadvantaged, and are without even minimal economic resources. Some medication requires significant spending from personal or family budgets, and people with epilepsy or family members are forced to decrease the dosage or stop taking AEDs.

It is likely that epilepsy care carries a high direct and indirect cost which may result in a significant individual and societal burden (Hong et al., 2009; Report by the All Party Parliamentary Group on Epilepsy, 2007). It could be argued that properly organized epilepsy care delivery throughout the country would have a significant positive impact on resources. Adequate treatment and care would be beneficial for people with epilepsy and their families, as well as for the socio-economic situation of the country.

During the epidemiological phase of this Demonstration Project valuable experience and information was gathered on the expenditure and human resources needed for a full package of epilepsy care. This is important for future planning of Demonstration Projects and also for policy makers

and health care authorities, in order to establish comprehensive systems of care and control of epilepsy.

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