# Using the Internet to recruit patients for Epilepsy Trials; results of a New Zealand Pilot Study.

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**Running Title:** Use of Internet for Epilepsy Trials

**Key Words:** Internet; Clinical Trials; Collaborative; Investigator-led; Non-commercial

Number of pages: 20

Words: 3975 (Title page, summary and paper)

Number of tables: 2 Proposed size, ¼ page each

Number of figures: 0

Number of references: 10**Abstract**

**Purpose:**

We created a database that could be accessed via the Internet by any neurologist or paediatric neurologist in New Zealand. The database was designed to facilitate recruitment of patients for investigator-driven drug trials.

**Methods:**

We established an epilepsy-database, and invited neurologists and paediatric neurologists throughout New Zealand to register patients via the Internet when uncertain of the optimal management. Details regarding seizure type and frequency, epilepsy syndrome, aetiology, drug history and investigations were collected. We produced an algorithm to select patients who had failed to respond to a single antiepileptic drug. These patients were randomised immediately via the Internet to receive a different drug. Participants were not reimbursed.

**Results:**

The pilot study recruited patients from mid June to December 2007. Sixteen neurologists participated; neurologists were based in eight different cities. 137 patients were registered, of whom 113 were considered suitable for drug trials. Thirty-five patients who had used a single antiepileptic drug (AED) were enrolled, and 14 of these were successfully randomised on-line to a different drug. Follow up information was entered via the Internet for all 108 patients who were seen again during the following year.

**Discussion:**

We have demonstrated that patients can be recruited for trials and randomised from routine clinics via the Internet. Trials could compare AEDs or look at other aspects of epilepsy management. An international pilot study is planned. Neurologists are invited to enrol patients with epilepsy, who would be suitable for randomised-controlled trials, into a web-based register.

**Key Words:** Internet; Clinical Trials; Collaborative; Investigator-led; Non-commercial

# Introduction

There is little high quality evidence to guide management decisions for patients with epilepsy. Many antiepileptic drugs (AEDs) have been shown to be superior to placebo, but few studies compare one AED with another. Relatively few studies consider patients with specific epilepsy syndromes or aetiologies.

Randomised controlled trials give the best evidence regarding respective merits of two or more treatments, since bias is eliminated. (Armitage and Berry, 1994) However, they generally require large numbers of participants, unless one treatment is very much more effective than the treatment(s) being compared. (Yusuf et al., 1984) For this reason, studies need to be multicentre, but these are difficult to organise and usually expensive to run. (Duley et al., 2008) If a study focuses on patients with uncommon syndromes, then it is even more difficult to recruit the number required to give the study adequate power.

The Internet provides the opportunity for large groups of researchers to collaborate to recruit the appropriate numbers of patients for these studies. By involving large numbers of doctors, it should be possible to recruit adequate numbers with uncommon conditions, since no single centre would need to recruit many subjects. (Bergin et al., 2007) Most neurologists see large numbers of patients for whom there is uncertainty regarding the optimal treatment, and if more of these patients could be recruited into clinical trials, the epilepsy community would be able to systematically address many of the current areas of uncertainty.

We set out to test whether it would be possible to enrol patients into randomised controlled trials from routine outpatient clinics at relatively little cost. We created a website and associated database, which could co-ordinate multiple different studies simultaneously. The aims of this pilot study were:

1. to assess the feasibility of recruitment of epilepsy patients from routine clinics via the internet, and
2. to see if these patients could be randomised for AED trials without any external funding.

# Methods:

We constructed a website and database that could be accessed by neurologists and paediatric neurologists from anywhere in New Zealand. We conducted a pilot study in which patients who had failed a single antiepileptic drug were randomised to receive one of several alternative drugs. Although no other patient group was randomised, doctors were encouraged to register any patient where there was more than one acceptable treatment option.

## The Website

Information sheets and consent forms were accessible from the website. Physicians had to confirm on the website that the patient had given consent before data could be entered into the database.

The website had several pages, each corresponding to a separate axis of information about the patient’s epilepsy. Drop-down lists and check boxes were used whenever possible. Pages were constructed in a hierarchical manner, so that doctors were faced with limited questions per page, but choosing a particular stem often opened up further options. These design features meant that precise information was collected easily and efficiently, yet the doctor was not overwhelmed with a large number of questions at the outset.

Data was encrypted and transmitted via the Internet to a secure website on a central server. Doctors had to be registered, and access to the website was password protected.

The website and questionnaire were designed so that it would be easy to specify a range of criteria to choose particular groups of patients; e.g. those with particular seizure types, epilepsy syndromes, aetiologies or drug use, or some combination of these (such as patients with complex partial seizures due to cavernous haemangiomas who were taking carbamazepine.)

## Demographic data

Patient name, sex, date of birth, hospital number and ethnicity were collected.

## Seizure types and Epilepsy Syndromes

Classification of seizure types and epilepsy syndromes was based on the ILAE classifications (Commission, 1981, Commission, 1989), though with minor modifications. It was possible to enter multiple seizure types per subject. For each seizure type, information regarding frequency and time of last seizure was requested.

## Aetiology

Aetiology was divided into the following major categories: unknown; idiopathic; acquired structural disease; congenital / genetic / developmental disorder; metabolic; drug toxicity; other. Choosing any option led to further choices which more precisely defined the aetiology. For instance, selecting ‘acquired structural disease’ brought up the following options: mesial temporal sclerosis; tumour; stroke; vascular malformation; trauma; infective; and degenerative. Choosing some of these options led to further subcategories being presented.

## Investigations

Information was requested regarding EEG, MRI, Video Monitoring, and histology. Doctors were asked to indicate whether EEGs were normal, or if they showed epileptiform discharges or other abnormalities; if epileptiform discharges were seen, were these generalised or focal, and if focal, where were the discharges located? In a similar manner, doctors indicated whether MRI scans were normal, showed abnormalities that were relevant to the epilepsy syndrome, or non-specific abnormalities. Again, doctors used drop-down boxes to indicate where the abnormalities were located.

## Drug History

Doctors were asked to indicate current and previous AEDs from a list of all AEDs available in New Zealand. They were also asked to indicate any AEDs that were not suitable for a particular patient. Information regarding drug side effects was also collected.

## Intercurrent Illnesses

On the final page of the questionnaire, information regarding intercurrent illnesses and non-AED medications was sought. The doctor was asked whether these illnesses or drugs would affect the possible choice of antiepileptic drugs for this patient. Finally, the doctor was asked whether this patient would be appropriate for a randomised controlled trial, or to choose from a list of possible reasons why the patient was not suitable.

## Demonstration Website

A demonstration website, which is not designed to store information on real patients, can be accessed until the end of 2010 to see how the process works. The website is: [www.epinetnz.co.nz/demo](http://www.epinetnz.co.nz/demo)

User name: epilepsy

Password: epilepsy

Readers should be aware, that since the pilot study has now been completed, the security certificate has lapsed. Browsers will therefore give a message to that effect. No information on real patients should therefore be transmitted.

### Randomisation Procedure

A computer algorithm determined whether the patient was eligible to be randomised to an AED for the second part of the study.

Patients who had failed their first AED were selected; in addition, patients had to meet the following criteria, as assessed by the neurologist:

* presently receiving either phenytoin, carbamazepine or sodium valproate;
* appropriate to change to another AED, either because of continuing seizures, or because of intolerable side effects;
* having epileptic seizures and not having non-epileptic seizures;
* compliant with previous treatment;
* suitable for treatment with at least 2 of the following drugs: sodium valproate, carbamazepine or lamotrigine;
* suitable for a randomised controlled trial, and;
* informed consent given to participate in a randomised controlled trial;

If the patient agreed to participate, then the patient was randomised immediately, and treatment was prescribed at the same visit. The potential AEDs to which the patient could be randomised varied, depending on the previous AED, the specific epilepsy syndrome and the seizure types. Patients with either absence or myoclonic seizures were randomised to either sodium valproate or lamotrigine, provided they had not already used either of these AEDs. All other patients were randomised to receive any of the 3 drugs they had not used previously.

Neither the treating neurologist nor the patient was blinded to the treatment. Guidelines for introducing the new AED and withdrawing the original AED were published on the website, but neurologists were free to do this according to their usual practice. Patients were asked to record their seizures in seizure diaries, which were brought to subsequent visits.

## Follow Up

Decisions regarding timing of follow up visits were left to the discretion and usual clinical practice of the recruiting doctor, except that at least one visit in the following year was required of patients who were randomised. Doctors were sent e-mails around the time they indicated they would be seeing the patient again, reminding them to fill in the follow-up questionnaire.

This pilot study was approved by the New Zealand Multi-region Ethics Committee. Patients were recruited between June and December 2007, and followed to December 2008.

**Recruitment of Investigators:**

Presentations outlining this study were made at the annual scientific meetings of the Neurological Association of New Zealand, and at the inaugural meeting of the New Zealand chapter of the ILAE. Neurologists at both meetings were invited to participate as co-investigators. In addition, all 40 neurologists and paediatric neurologists practising in New Zealand were also invited to participate by e-mail.

## Results

**Doctors:**

Thirty adult and paediatric neurologists agreed to participate, and were registered as users of the site. Sixteen of these neurologists from 8 different cities enrolled patients. Participating doctors registered between 1 and 38 patients each. Participating neurologists are listed at the end of this paper.

After familiarisation with the website, it took doctors 6 – 8 minutes to enter data on an average new patient. More complex patients, for whom notes had to be searched to find the relevant information, required up to 20 minutes for data entry.

**Patients:**

One hundred and thirty seven patients were registered via the website (Table 1). Ages ranged from 1 month to 78 yr. Sixty patients were male, and 77 female. Fifty patients had generalised seizures, and 99 had partial seizures. The epilepsy was considered idiopathic in 30 patients, secondary to acquired structural disease in 49, and secondary to congenital, genetic, or development disorders in 10. The aetiology was unknown in 48 patients. Ten patients had not been treated with AEDs. One hundred and thirteen patients were considered suitable for drug trials.

Thirty five patients who had used a single AED were enrolled; of these, 14 patients were successfully randomised on line in the second part of the study to receive a different drug. These patients had previously used phenytoin (4), carbamazepine (7), and sodium valproate (3). Twenty-one patients were not randomised for various reasons. (Table 1) Six patients could not be entered in the trial because only one of the three potential AEDs to which they could be randomised was considered suitable.

Randomisation resulted in the following: 10 of 14 patients eligible for lamotrigine received lamotrigine; 3 of 7 patients eligible for carbamazepine received carbamazepine; and 1 of 10 patients eligible for sodium valproate received sodium valproate. (Table 2)

**Follow-up data:**

All 16 participating neurologists provided follow up data on their patients.

Eighteen of the 137 patients were discharged from the clinic at the time they were enrolled, and no follow up was recorded. Follow up information was entered into the database on 108 of the remaining 119 patients; more than one follow up was submitted for 19 patients.

Eight patients failed to attend their follow up appointment, and were discharged from the clinic. The investigators were informed of this outcome by e-mail in all circumstances. Three patients had not been seen for follow up by December 31, 2008.

**Discussion:**

We have constructed a website and database to facilitate randomised controlled trials, and have demonstrated that physicians and patients from multiple locations will participate in this type of study. Research using this approach can be performed simply and cheaply from routine epilepsy outpatient clinics. For the purposes of the pilot study, we established an algorithm to randomise to a different AED those patients who had failed to respond to their first AED. Although we only randomised 14 patients, we have demonstrated that this approach is feasible.

Nearly three quarters of the neurologists and paediatric neurologists in New Zealand indicated a willingness to participate and registered to use the website, though only just over one half of these actually did so. All the doctors who initially registered patients also provided follow up. Although eight patients were lost to follow up, their doctors informed the investigators of this outcome when they were prompted by e-mail.

New Zealand has a population of only 4 million people, and it would not be possible to recruit sufficient numbers of patients to answer questions regarding the optimal treatment of patients with epilepsy. This project was a proof-of-concept study to test the feasibility of recruitment for clinical trials using the Internet, and we knew we would not actually determine which of several alternative AEDs is the best treatment. We chose to randomise this particular patient group because we wanted a certain degree of complexity in the algorithm we wrote to select patients and allocate treatment. We selected patients who had received either phenytoin, carbamazepine or sodium valproate because at the time the study commenced, these were the 3 drugs that were used most frequently as monotherapy in New Zealand. In June 2007, the New Zealand Ministry of Health did not fund lamotrigine, topiramate, gabapentin or levetiracetam as initial treatment.

The strength of this web-based approach is that it could potentially involve a wide range of neurologists and paediatric neurologists around the world – essentially, any approved doctor with sufficient expertise and enthusiasm, and access to the Internet. By involving large numbers of doctors, it would be possible to enrol large numbers of patients relatively rapidly. It would also facilitate collection of groups of patients with uncommon epilepsy syndromes.

We are now modifying the platform we have created so that it can be accessed by doctors from other countries. We would like to establish a network of neurologists and paediatric neurologists from multiple centres world-wide who are interested in conducting trials using this approach. We have received funding to proceed with the next phase of the project, and hope to have a multinational study underway later in 2009. We will not be entering patients into randomised controlled trials at this stage, but will be using our revised platform to collect patient data into registries, with the idea of undertaking observational cohort studies.

Our ultimate aim is to create an international environment where epileptologists check on a website to see if patients can be enrolled in randomised controlled trials whenever there is a situation of equipoise – i.e., whenever it is unclear which of several possible treatments is optimal. Clearly, many people will never be suitable for randomised controlled trials, and there will not be trials underway for many other patients who might be suitable. However, we believe that it would be possible to set up multiple randomised controlled trials running in parallel using the approach tested in this pilot study. It would be possible to select patient groups with quite specific characteristics and to conduct trials confined to patients with particular aetiologies or epilepsy syndromes. We envisage that these trials would be independent of pharmaceutical companies, and could be initiated from any of the participating centres. However, there are further complexities and expenses involved in running randomised controlled trials compared with observational studies, and we will work towards this goal in a series of small steps.

Our study was unblinded, but still obtained the benefits of randomisation. This has been the approach used by many influential studies, such as the SANAD trials. (Marson et al., 2007a, Marson et al., 2007b) It would be possible (though more difficult) to perform double-blind trials using the same platform. However, we see this platform as being of particular value in performing trials that are unlikely to be performed in a double-blind manner, such as comparing specific combinations of drugs. We think this platform would be ideal to study non-medicinal treatments, or to study other management decisions, such as the use of EEG in determining whether to discontinue AED treatment.

If this project is to be successful, it is essential that the data entered is accurate; moreover, there needs to be confidence among the epilepsy community on this point, if results that come from the project are to be credible. On the one hand, we wish to encourage participation by as many doctors as possible, to enhance recruitment of patients; on the other hand, we wish to restrict data entry to those who are clearly knowledgeable about epilepsy. We have not yet fully resolved this tension. It is relatively easy to incorporate checklists into the software to ensure that entries are internally consistent. It will also be possible to ask investigators to send copies of original reports to a central registry if this is considered necessary for a particular study. We anticipate that there will be some form of central data monitoring and auditing, but we have not yet finalised arrangements for this. However, we believe that many more neurologists could participate in clinical research than do so at present; indeed, we are of the view that many epileptologists would willingly participate if they could do so relatively easily. We were struck by the enthusiasm of the patients that we approached for this pilot study. We acknowledge, though, that there will need to be steps that ensure that all those who want to be co-investigators have adequate knowledge of epilepsy and speak the same language.

In our pilot study, all data had to be entered by a neurologist or paediatric neurologist; we included this restriction in an effort to ensure high standards of data-entry. This restriction is probably not necessary. In the platform we are now developing, it will be possible for data to be entered by clinical assistants, though only approved physicians or research co-ordinators will be able to submit the form after confirming the accuracy of the data. It will be possible to interrupt the data entry and ‘park’ the form, so that data can be entered at a later date.

Epilepsy is not a static condition, and epilepsy syndromes sometimes evolve. Further information may become available that results in a change in diagnosis or provides new knowledge regarding the aetiology. At times, there is genuine uncertainty regarding the nature of a patient’s condition. It will be possible to change the diagnosis in the database as new information is obtained. It will be easy to correct errors in the data-entry itself. However, a record of earlier entries will be kept for audit purposes, and to ensure that an accurate record of an individual patient’s history is maintained.

We have designed the platform so that participation will benefit patients and their doctors, even if the patient is not entered into a trial. Whenever doctors log on for a particular patient, they will receive a summary of the patient’s previously entered seizure and drug history, and results of investigations. If a patient’s diagnosis changes, then this information will be apparent in the summary, so that clinical uncertainties are not ignored. This information will be updated with every subsequent patient visit. The summary can be printed out, put in the notes, sent to general practitioners, or given to patients. We have received feedback from doctors participating in the New Zealand pilot study indicating that some doctors would participate primarily for this reason.

We have structured the database so that physicians will have access to information for all their patients. This will therefore function as a personal database. If the patients agree, then other physicians working at that centre will also be able to access this data. The database will function as a prospective register, so that it will be possible for researchers to review anonymised data from larger cohorts of patients, even in patient groups who have not been entered into trials. However, investigators will not have access to any identifying personal data on patients from other centres. An international steering committee would be established to oversee such research projects.

It is critical that all patient data is completely secure, and that patients, investigators and health authorities all have confidence in this fact. For the pilot study, we used a secure website, and all personal data was encrypted. Doctors could not enter any information on a patient without the patient’s explicit and informed consent. The website was password protected, and only approved users could access it. We intend that all these safety features are also included in future phases of the project. In addition, for all subsequent phases of the project, the database will be situated on a server that is on a separate local area network (LAN). These security measures meet or exceed those that are usually required for transmission of confidential personal data.

We are not aware of any similar approach to the use of the Internet to recruit patients with epilepsy for trials. Others have certainly used the Internet; for example, the International Collaborative Infantile Spasms Study uses the Internet to recruit and randomise patients, though follow up data is not entered on-line, and the website is dedicated to investigating a single condition. (ICISS, 2009) Koenig and colleagues have constructed a database on a central server that can be accessed by neurologists and paediatric neurologists from multiple centres. (Koenig et al., 2007) They hope that such a database will enable observational data on large numbers of patients with various epilepsy syndromes to be gathered prospectively. We see their approach as complementary to ours. However, we are not aware of any intention by these workers to use their database to coordinate randomised controlled trials.

We would invite neurologists and paediatric neurologists who are interested in participating in further development of this project to contact us.

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**Acknowledgements:**

Funding for this project was provided by a grant from the Julius Brendel trust, and by means of a summer student scholarship from the Computer Science Department at the University of Auckland.

None of the authors has any conflict of interest to disclose

We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.**References**

Armitage, P. & Berry, G. (1994) *Statistical methods in medical research,* Oxford Blackwell.

Bergin, P., Frith, R., Walker, E. & Timmings, P. (2007) How to get the answer to nearly everything: using the internet for epilepsy research. *Epilepsia,* 48**,** 1415-7; discussion 1417-24.

Commission on Classification and Terminology of the International League Against Epilepsy. (1981) Proposal for revised clinical and electroencephalographic classification of epileptic seizures. *Epilepsia,* 22**,** 489-501.

Commission on Classification and Terminology of the International League Against Epilepsy. (1989) Proposal for revised classification of epilepsies and epileptic syndromes. Commission *Epilepsia,* 30**,** 389-99.

Duley, L., Antman, K., Arena, J., Avezum, A., Blumenthal, M., Bosch, J., Chrolavicius, S., Li, T., Ounpuu, S., Perez, A. C., Sleight, P., Svard, R., Temple, R., Tsouderous, Y., Yunis, C. & Yusuf, S. (2008) Specific barriers to the conduct of randomized trials. *Clin Trials,* 5**,** 40-8.

ICISS (2009) The International Collaborative Infantile Spasms Study (ICISS) <http://www.bath.ac.uk/health/research/iciss/index2.php>. Accessed 22 April 2009.

Koenig, S. A., Dobson, P., Longin, E., Michalec, D., Gerstner, T. & Taylor, J. (2007) Internet-based knowledge management database for children and adults with epilepsy: a possible model project for evidence-based medicine in the future. *Seizure,* 16**,** 703-8.

Marson, A. G., Al-Kharusi, A. M., Alwaidh, M., Appleton, R., Baker, G. A., Chadwick, D. W., Cramp, C., Cockerell, O. C., Cooper, P. N., Doughty, J., Eaton, B., Gamble, C., Goulding, P. J., Howell, S. J., Hughes, A., Jackson, M., Jacoby, A., Kellett, M., Lawson, G. R., Leach, J. P., Nicolaides, P., Roberts, R., Shackley, P., Shen, J., Smith, D. F., Smith, P. E., Smith, C. T., Vanoli, A. & Williamson, P. R. (2007a) The SANAD study of effectiveness of carbamazepine, gabapentin, lamotrigine, oxcarbazepine, or topiramate for treatment of partial epilepsy: an unblinded randomised controlled trial. *Lancet,* 369**,** 1000-15.

Marson, A. G., Al-Kharusi, A. M., Alwaidh, M., Appleton, R., Baker, G. A., Chadwick, D. W., Cramp, C., Cockerell, O. C., Cooper, P. N., Doughty, J., Eaton, B., Gamble, C., Goulding, P. J., Howell, S. J., Hughes, A., Jackson, M., Jacoby, A., Kellett, M., Lawson, G. R., Leach, J. P., Nicolaides, P., Roberts, R., Shackley, P., Shen, J., Smith, D. F., Smith, P. E., Smith, C. T., Vanoli, A. & Williamson, P. R. (2007b) The SANAD study of effectiveness of valproate, lamotrigine, or topiramate for generalised and unclassifiable epilepsy: an unblinded randomised controlled trial. *Lancet,* 369**,** 1016-26.

Yusuf, S., Collins, R. & Peto, R. (1984) Why do we need some large, simple randomized trials? . *Stat Med* 3**,** 409–420.

**Table 1: Patients entered into the database who had used a single AED**

|  |  |
| --- | --- |
| Patients successfully randomised | 14 |
| Considered not suitable by referring doctor (non-compliance / behavioural issues) | 6 |
| Seizures adequately controlled or neurologist did not consider randomisation appropriate | 7 |
| Patient did not consent | 1 |
| Patient not currently taking an AED | 2 |
| Diagnosis unclear | 3 |
| Only 1 of the 3 possible AEDs deemed suitable | 6 |
|  |  |
| Total | 35\* |

\* Some patients had more than one reason for non-randomisation

**Abbreviations:**

AED anti epileptic drug

### Table 2: Details of patients who were successfully randomised

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Patient** | **AED used** | **Epilepsy syndrome** | **AEDs available** | **AED allocated** |
| 6 | CBZ | IGE-JME | SVA, LTG | LTG |
| 44 | SVA | LRE-TLE, NOS | CBZ, LTG | CBZ |
| 47 | CBZ | EU | SVA, LTG | LTG |
| 69 | PHT | LRE-Crypt | CBZ, SVA, LTG | CBZ |
| 93 | CBZ | LRE-FLE | SVA, LTG | LTG |
| 94 | CBZ | LRE-S, NOS | SVA, LTG | LTG |
| 107 | SVA | LRE-Crypt | CBZ, LTG | CBZ |
| 109 | CBZ | LRE-Crypt | SVA, LTG | LTG |
| 114 | PHT | LRE-NOS | CBZ, SVA, LTG | LTG |
| 125 | CBZ | LRE-OLE | SVA, LTG | LTG |
| 132 | PHT | LRE-NOS | CBZ, SVA, LTG | LTG |
| 133 | PHT | LRE-Crypt | CBZ, SVA, LTG | LTG |
| 134 | SVA | LRE-S, NOS | CBZ, LTG | LTG |
| 145 | CBZ | LRE-TLE, NOS | SVA, LTG | SVA |

## Abbreviations

*Drugs:* AED anti epileptic drug; CBZ carbamazepine; LTG lamotrigine; PHT phenytoin; SVA sodium valproate

*Epilepsy syndromes:* Crypt cryptogenic (presumed symptomatic, aetiology unclear); EU epilepsy undetermined if focal or generalised; FLE frontal lobe epilepsy; IGE idiopathic generalised epilepsy; JME juvenile myoclonic epilepsy; LRE localisation related epilepsy; NOS not otherwise specified; OLE occipital lobe epilepsy; S symptomatic; TLE temporal lobe epilepsy