Version: 1
Date: 1th August 2014

STUDY PROCEDURE

Title: "GLOBAL AUDIT OF TREATMENT OF REFRACTORY STATUS EPILEPTICUS"

Promoter Center: UCL Institute of Neurology, National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG, Great Britain.

Steering committee: Simon Shorvon, Eugen Trinka, Monica Ferlisi, Sara Hocker.

1. Introduction and Background

Tonic–clonic status epilepticus is a medical emergency. Treatment is aimed at stopping seizures largely in order to avoid cerebral damage and other morbidity. All contemporary protocols take a staged approach to treatment. Typically, in Stage 1 (early status epilepticus), therapy is with benzodiazepines. If seizures continue despite this therapy, the patient is said to be in Stage 2 (established status epilepticus) and therapy is with intravenous anti-epileptic drugs such as phenytoin, phenobarbital or valproate. If seizures continue despite this treatment for up to 2 h, the patient is said to be in Stage 3 (refractory status epilepticus) and general anaesthesia is usually recommended, at a dose that results in EEG burst suppression (a level of anaesthesia at which all seizure activity is usually controlled). In most patients, this treatment regimen is sufficient to control the seizures. In some though seizures continue or recur. Super-refractory status epilepticus is defined as status epilepticus that continues or recurs 24 h or more after the onset of anaesthetic therapy, including those cases that recur on the reduction or withdrawal of anaesthesia. It was a term used first in the Third London-Innsbruck Colloquium on status epilepticus held in Oxford on 7–9th April 2011 (Shorvon and Trinka, 2011). In the series of 35 patients of Holtkamp et al. (2005), seven (20%) recurred within 5 days of tapering the anaesthetic drug and in all other studies at least 50% of those requiring anaesthesia will become super-refractory. From the published findings, it can be estimated that 15% of all the cases with status epilepticus admitted to hospital will become super-refractory. All neurologists are likely to be involved with the care of patients with refractory and super-refractory status epilepticus, or consulted by their intensivist colleagues about how best to proceed in this situation. The treatment of this issue is a terra incognita from the point of view of evidence-based medicine, yet a landscape where action is required. Refractory and super-refractory status epilepticus are serious conditions. The mortality rate is substantial, reported in various series between 30 and 50%. Yet, despite the fact that it remains an important clinical problem in all neurology centres worldwide, for many therapies, and treatment approaches, there is a remarkable lack of published data concerning effectiveness, safety or outcome. A great number of therapies are in current usage and the literature reporting these therapies has been reviewed recently (Shorvon and Ferlisi, 2011). The therapies considered include thiopental, pentobarbital, midazolam,

propofol, ketamine, inhalational anaesthetics (isoflurane, desflurane), antiepileptic drugs (topiramate, lacosamide, pregabalin, levetiracetam), hypothermia, magnesium, pyridoxine, immunotherapy, ketogenic diet, emergency neurosurgery, electroconvulsive therapy (ECT), CSF drainage, vagal nerve stimulation and deep brain stimulation. This recent review point out that there is only one randomized or controlled study of any of these therapies (a trial comparing thiopental and midazolam). However, the trial required 150 patients for adequate power and recruited only 24 patients (Rosetti et al., 2011). Apart from this, the evidence base consists entirely of single case reports or small series. None of the widely recommended drugs or treatment approaches has been subjected to any sort of systematic review, despite their adoption worldwide. This is an unsatisfactory state of affairs. Assessing outcome of individual therapies is even more difficult due to the complete lack of controlled data, the fact that all super-refractory patients are on multiple therapies, the tendency for authors to report effects days after the therapy is started and which can therefore be difficult to securely attribute to the therapy (Ferlisi and Shorvon, 2012), and the fact that outcome fundamentally depends on the underlying aetiology, which differs in different studies (Neligan and Shorvon, 2010). The lack of evidence and the lack of outcome data in this situation require urgent remediation. Randomized or controlled studies that are sufficiently powered are not feasible in relation to the many therapies and treatment approaches discussed above. For this reason, we propose a multinational database of therapies used in refractory and super-refractory cases and their outcome. Only with such a database can evidence of effectiveness be gathered and progress made in this uncommon but difficult clinical situation.

2. Aim of the audit

The aim of a multinational audit is to collect data on the range of therapies used in the stage of refractory/super-refractory status epilepticus, the relative frequency of their usage and their outcome. Additional information will be collected about the etiology of status epilepticus. The aim is then to document what treatments of refractory status epilepticus are being used in clinical practise around the world, and also information on aetiology and outcome of this serious condition. The review will form the basis for the formulation of clinical guidelines and to point to areas of future research.

3. Inclusion Criteria

Case definition: Refractory status epilepticus is defined as ‘status epilepticus requiring general anaesthesia in an ITU setting’. Super-refractory status epilepticus is defined as those cases not responding to initial anaesthesia (see introduction for references).

4. Method:

Data will be collected on a multi-national basis by active surveillance. Doctors from different countries, involved in the care of patients with status epilepticus, will be asked to participate in the audit: every time they treat a patient with refractory/super-refractory status epilepticus (as defined above), they are asked to complete an online audit questionnaire forms. No patient personal identifiers (i.e. : name, surname) will be included, and the name of the hospital in which the patient is treated is also optional.

(a) Participants: Those who have agreed to participate are part of a worldwide study team. They are doctors involved in the care of patients with status epilepticus. They are asked to complete the online forms for all patients they encounter with refractory status epilepticus on a prospective basis.

(b) Active surveillance: Every month, each participant will be sent a standard email, asking if a case has been seen in the previous month. The doctor will be asked to click on a button marked 'Yes' or 'No'. If the answer is 'Yes' an online proforma will appear (see below) to be completed (which should take less than 5 mins to complete).

(c) Organisation: Centres are organized into national groupings, with lead contacts in each grouping to answer queries and to assist if required.

(d) Ethics approvals: As this is an audit, with no intervention of any sort by the study team and no collection of patient identifiers, in most countries there will be no need for ethics approval or patient consent. If ethics approval is required, the study team will assist in the completion of relevant forms.

(e) Written consent: If written consent is required (in most countries this is not required), and as the patients are by definition unconscious at time of first questionnaire, consent will be asked for in retrospect. If consent is then refused, the questionnaires will be destroyed and an email will be sent to SoSci Survey asking for deleting all the data referring to a particular ID.

5. Data collection:

Questionnaire 1 to be completed by the participating doctor (see attachment, Questionnaire 1). Then the doctor will receive after 2 weeks another mail, asking for the completion of short follow up

questionnaires (see attachment, Questionnaire 2-follow up), until the patient is no longer on the ICU, when an outcome questionnaire is sent (Questionnaire 3, see attachment).
Finally, a follow-up questionnaire will be sent after 3 and 6 months to be completed (see attachment, Questionnaire 4).

6. Confidentiality

The audit will not have access to the name or other patient identifier, nor the name of the hospital at which the patient was treated. It's responsibility of each participating doctor to keep a separate file containing patient personal data (name, surname, date of birth) and the patient's identification number (specific for each participating doctor).

7. Data management

All the data, collected in anonymised fashion through the on-line questionnaires, will be managed by SoSci Survey, Marinne-Brandt-Strabe 29, 80807 Munchen, a software package who created the online questionnaires. This software can also provide computation of descriptive statistics:

- Demographic data (%, stratified by status type)
- Details of status (% stratified by demographics)
- Range of treatments (stratified by duration/status type/demographics)
- Combinations of treatments (stratified by duration/status type/demographics)
- Time of treatments (%, stratified by status type)
- Outcome of treatments (stratified by duration/status type/demographics)

The data will not be released to any outside body orperson, but will be retained only by the study team.

8. Access to data and data property:

Access to the study data is restricted to the members of the steering committee.

9. Publication policy

All doctors who contribute to the study will be recognised. Authorship will follow the policy of the Vancouver Protocols.

References

Shorvon SD, Trinka E. Proceedings of the 3rd London-Innsbruck Colloquium on Status Epilepticus. Epilepsia 2011; 52 (Suppl 5).

Holtkamp M, Othman J, Buchheim K, Meierkord H. Predictors and prognosis of refractory status epilepticus treated in a neurological intensive care unit. J Neurol Neurosurg Psychiatry 2005; 76: 534–9.

Shorvon S, Ferlisi M. The treatment of super-refractory status epilepticus: a critical review of available therapies and a clinical treatment protocol. Brain 2011; 134: 2802–18.

Rossetti AO, Milligan TA, Vulliemoz S, Michaelides C, Bertschi M, Lee JW. A randomized trial for the treatment of refractory status epilepticus. Neurocrit Care 2011; 14: 4–10.

Neligan A, Shorvon SD. Frequency and prognosis of convulsive status epilepticus of different causes: a systematic review. Arch Neurol 2010; 67: 931–40.

Ferlisi M, Shorvon S. The outcome of therapies in refractory and super-refractory convulsive status epilepticus and recommendations for therapy. Brain 2012; 135: 2314-28.

Version: 1
Date: 1th August 2014

QUESTOINNAIRE 1

FIRST QUESTIONNAIRE

QUESTION	TYPE OF FIELD	EXAMPLE
SCREEN 1 - DEMOGRAPHICS		
Date	Calendar	1.1.2012
Name of doctor filling in form	Free text – but converted into number by computer	*John Smith*
Name of hospital	Free text – but converted into number by computer	*National Hospital, London*
Patient age	Age in years	*16*
	Months (if <1 year)	*3*
Country	Drop down menu - see (n) below	
Patient gender	Drop down menu – see (a) below	*Male*
SCREEN 2 – DETAILS OF STATUS EPILEPTICUS		
Prior history of epilepsy	Drop down menu – see [c] below	*Yes*
Cause of status epilepticus	Drop down menu – see (d) below	*Encephalitis*
Type of status epilepticus	Drop down menu – see (e) below	*Convulsive*
Duration of status epilepticus before any treatment	Drop down menu – see (m) below	*<1 hour*
Duration of status epilepticus before first anaesthetic administered	Drop down menu – see (b) below	*More than 14 days*
SCREEN 3 – ANAESTHETICS		
First anaesthetic therapy used	Drop down menu – see (f) below	*Propofol*
Duration of use of first anaesthetic	Drop down menu – see (g) below	*1 day*
Second anaesthetic therapy used	Drop down menu – see (f) below	*Thiopental*
Duration of use of second anaesthetic	Drop down menu – see (g) below	*3 days*
Third anaesthetic therapy used	Drop down menu – see (f) below	*Midazolam*
Duration of use of third	Drop down menu –	*10 days*

anaesthetic	see (g) below	
Fourth anaesthetic therapy used	Drop down menu – see (b) below	*Ketamine*
Duration of use of fourth anaesthetic	Drop down menu – see (c) below	*5 days*
SCREEN 4 - ANTIEPILEPTICS		
Antiepileptics and duration of therapy	Drop down menu – see (h) below	*Phenytoin – 3 days* *Phenobarbital - 5 days* *Topiramate – Still being treated with this drug*
Order of use of drugs	Drop down menu generated from answers in (h) – see (i) below	*1st Phenobarbital* *2nd Phenytoin*
SCREEN 5 – OTHER THERAPIES		
Other therapies	Drop down menu – see (j) below	*Hypothermia* *Ketogenic diet* *Magnesium*
Duration of therapies	Drop down menu generated from answers in (j)– see (k) below	*Hypothermia – 10 days* *Ketogenic – Still being treated with this therapy* *Magnesium – one-off therapy*
Order in which tried	Drop down menu generated from answers in (j) - see (l) below	*1st Hypothermia* *2nd Magnesium* *3rd Ketogenic diet*

DROP DOWN MENUS

a	Male Female

b	Less than 1 hour Less than 1 day Longer than 1 day Don't know

c	Yes No Don't know

d	Unknown (cryptogenic) Vascular (incl. stroke) Anoxic (incl. cardiac arrest) Trauma Acute encephalitis

	Acute meningitis Other infection (specify – free text box) Alcohol Other toxins (specify – free text box) Metabolic (specify – free text box) Cerebral tumour Antiepileptic drug reduction/withdrawal Genetic/chromosomal (specify – free text box) Immunological – NMDA receptor Antibodies + Immunological – VGKA Antibodies + Immunological – Lupus (seropositive) Immunological – other (specify – free text box) Mitochondrial disease (specify – free text box) Other (specify – free text box)

e	Convulsive (including tonic-clonic SE) Nonconvulsive (specify – free text box) Convulsive evolving to nonconvulsive Other (specify – free text box) Don't know

f	Propofol Thiopental Pentobarbital Midazolam Ketamine Inhalational anaesthetics (specify – free text box) Other (specify – free text box) None Don't know

g	Still being treated with this drug 24 hours or less 1-7 days 8-14 days More than 14 days (specify – free text box) Other (specify – free text box) Don't know

h	Phenytoin Phenobarbital Valproate Levetiracetam Carbamazepine Clonazepam Clobazam Other benzodiazepine (specify – free text box)

	Topiramate Lamotrigine Oxcarbazepine Pregabalin Gabapentin Zonisamide Lacosamide Retigabine Perampenil Vigabatrin Other (specify – free text box) None Don't know

i	1st 2nd 3rd 4th 5th 6th Don't know (the list generated from answers to (h)

j	Hypothermia Neurosurgery (specify type – free text box) Steroids IVIg Plasma exchange Ketogenic diet Electroconvulsive therapy (ECT), course of Vagal nerve stimulation (VNS) Transcranial magnetic stimulation (TMS). course of Other (specify – free text box) None Don't know

k	Still being treated with this therapy On-off therapy 24 hours or less 1-7 days 8-14 days More than 14 days (specify – free text box) Other (specify – free text box) Don't know (the list generated from answers to (j)

Version: 1
Date: 1th August 2014

l	1st 2nd 3rd 4th 5th 6th Don't know (the list generated from answers to (j)

m	1 hour or less 1-6 hours 6-12 hours 12-24 hour 1-7 days >7 days Other (specify – free text box) Not known

n	193 = Afghanistan 355 = Albania 213 = Algeria 1684 = American Samoa 376 = Andorra 244 = Angola 1264 = Anguilla 672 = Antarctica 1268 = Antigua and Barbuda 54 = Argentina 374 = Armenia 297 = Aruba 61 = Australia 43 = Austria 994 = Azerbaijan 1242 = Bahamas 973 = Bahrain 880 = Bangladesh 1246 = Barbados 375 = Belarus 32 = Belgium 501 = Belize 229 = Benin 1441 = Bermuda 975 = Bhutan 591 = Bolivia 387 = Bosnia and Herzegovina 267 = Botswana

Version: 1
Date: 1th August 2014

	55 = Brazil 1284 = British Virgin Islands 673 = Brunei 359 = Bulgaria 226 = Burkina Faso 95 = Burma (Myanmar) 257 = Burundi 855 = Cambodia 237 = Cameroon 8001 = Canada 238 = Cape Verde 1345 = Cayman Islands 236 = Central African Republic 235 = Chad 56 = Chile 86 = China 8061 = Christmas Island 9061 = Cocos (Keeling) Islands 57 = Colombia 269 = Comoros 682 = Cook Islands 506 = Costa Rica 385 = Croatia 53 = Cuba 357 = Cyprus 420 = Czech Republic 243 = Democratic Republic of the Congo 45 = Denmark 253 = Djibouti 1767 = Dominica 1809 = Dominican Republic 593 = Ecuador 20 = Egypt 503 = El Salvador 240 = Equatorial Guinea 291 = Eritrea 372 = Estonia 251 = Ethiopia 500 = Falkland Islands 298 = Faroe Islands 679 = Fiji 358 = Finland 33 = France 689 = French Polynesia 241 = Gabon 220 = Gambia 9970 = Gaza Strip 995 = Georgia 49 = Germany 233 = Ghana 350 = Gibraltar 30 = Greece

Version: 1
Date: 1th August 2014

	299 = Greenland 1473 = Grenada 1671 = Guam 502 = Guatemala 224 = Guinea 245 = Guinea-Bissau 592 = Guyana 509 = Haiti 9039 = Holy See (Vatican City) 504 = Honduras 852 = Hong Kong 36 = Hungary 354 = Iceland 91 = India 62 = Indonesia 98 = Iran 964 = Iraq 353 = Ireland 9044 = Isle of Man 972 = Israel 39 = Italy 225 = Ivory Coast 1876 = Jamaica 81 = Japan 962 = Jordan 9007 = Kazakhstan 254 = Kenya 686 = Kiribati 381 = Kosovo 965 = Kuwait 996 = Kyrgyzstan 856 = Laos 371 = Latvia 961 = Lebanon 266 = Lesotho 231 = Liberia 218 = Libya 423 = Liechtenstein 370 = Lithuania 352 = Luxembourg 853 = Macau 389 = Macedonia 261 = Madagascar 265 = Malawi 60 = Malaysia 960 = Maldives 223 = Mali 356 = Malta 692 = Marshall Islands 222 = Mauritania 230 = Mauritius 262 = Mayotte

Version: 1
Date: 1th August 2014

	52 = Mexico 691 = Micronesia 373 = Moldova 377 = Monaco 976 = Mongolia 382 = Montenegro 1664 = Montserrat 212 = Morocco 258 = Mozambique 264 = Namibia 674 = Nauru 977 = Nepal 31 = Netherlands 599 = Netherlands Antilles 687 = New Caledonia 64 = New Zealand 505 = Nicaragua 227 = Niger 234 = Nigeria 683 = Niue 9672 = Norfolk Island 850 = North Korea 1670 = Northern Mariana Islands 47 = Norway 968 = Oman 92 = Pakistan 680 = Palau 507 = Panama 675 = Papua New Guinea 595 = Paraguay 51 = Peru 63 = Philippines 870 = Pitcairn Islands 48 = Poland 351 = Portugal 9001 = Puerto Rico 974 = Qatar 242 = Republic of the Congo 40 = Romania 7 = Russia 250 = Rwanda 590 = Saint Barthelemy 290 = Saint Helena 1869 = Saint Kitts and Nevis 1758 = Saint Lucia 1599 = Saint Martin 508 = Saint Pierre and Miquelon 1784 = Saint Vincent and the Grenadines 685 = Samoa 378 = San Marino 239 = Sao Tome and Principe 966 = Saudi Arabia

Version: 1
Date: 1th August 2014

	221 = Senegal 9381 = Serbia 248 = Seychelles 232 = Sierra Leone 65 = Singapore 421 = Slovakia 386 = Slovenia 677 = Solomon Islands 252 = Somalia 27 = South Africa 82 = South Korea 34 = Spain 94 = Sri Lanka 249 = Sudan 597 = Suriname 268 = Swaziland 46 = Sweden 41 = Switzerland 963 = Syria 886 = Taiwan 992 = Tajikistan 255 = Tanzania 66 = Thailand 670 = Timor-Leste 228 = Togo 690 = Tokelau 676 = Tonga 1868 = Trinidad and Tobago 216 = Tunisia 90 = Turkey 993 = Turkmenistan 1649 = Turks and Caicos Islands 688 = Tuvalu 256 = Uganda 380 = Ukraine 971 = United Arab Emirates 44 = United Kingdom 1 = United States 598 = Uruguay 1340 = US Virgin Islands 998 = Uzbekistan 678 = Vanuatu 58 = Venezuela 84 = Vietnam 681 = Wallis and Futuna 970 = West Bank 967 = Yemen 260 = Zambia 263 = Zimbabwe

Version: 1
Date: 1th August 2014

QUESTOINNAIRE 2

FOLLOW UP QUESTIONNAIRE

QUESTION	TYPE OF FIELD	EXAMPLE
SCREEN 1 – REITERATION OF DEMOGRAPHIC AND TYPE OF STATUS EPILEPTICUS AND TREATMENTS REPORTED IN FIRST QUESTIONNAIRE – On – [date] *Date reported : 1.1.2012* *Reporting doctor: John Smith* *Hospital: National Hospital London* *Patient age: 16 years* *Patient gender: Male* *Duration of status epilepticus before first treatment: <1 hour* *Duration of status epilepticus before first anaesthetic administered: 14 days* *Prior History of epilepsy: Yes* *Cause of status epilepticus: Encephalitis* *Type of status epilepticus: Convulsive* Therapy reported by [date] – *Anaesthetics – Propofol for 1 day, thiopental for 3 days and midazolam for 10 days* – *Antiepileptics – Phenytoin – 3 days* *Phenobarbital – 5 days* *Topiramate – Still being treated with this drug* – *Order of use – 1st Phenobarbital , 2nd Phenytoin* – *Other therapies – Hypothermia – 10 days* *Ketogenic – Still being treated with this therapy* *Magnesium – one-off therapy* – ***Order of use –*** *1st Hypothermia* *2nd Magnesium, 3rd Ketogenic diet* **Then the questions below**		
Date	Calendar	13.1.2012
Name of doctor filling in form	Free text – but converted into number by computer	*John Smith*
Are there any amendments or changes to this information ? please specify	Free text box	*Cause of status shown to be stroke not encephalitis*
What is the current status of therapy, as far as you are aware	Drop down menu (a)	*Yes – continuing intensive therapy*
SCREEN 2 – ANAESTHETICS		
Since last report, please specify anaesthetics used		
First anaesthetic therapy used	Drop down menu – see (b) below	*Propofol*
Duration of use of first anaesthetic	Drop down menu – see (c) below	*I day*

Second anaesthetic therapy used	Drop down menu – see (b) below	*Thiopental*
Duration of use of second anaesthetic	Drop down menu – see (c) below	*3 days*
Third anaesthetic therapy used	Drop down menu – see (b) below	*Midazolam*
Duration of use of third anaesthetic	Drop down menu – see (c) below	*10 days*
Fourth anaesthetic therapy used	Drop down menu – see (b) below	*Ketamine*
Duration of use of fourth anaesthetic	Drop down menu – see (c) below	*5 days*
SCREEN 3 - ANTIEPILEPTICS		
Since last report, please specify antiepileptics used		
First Antiepileptic used	Drop down menu – see (d) below	*Phenytoin*
Duration of use of first antiepileptic	Drop down menu – see (e) below	*3 days*
Second Antiepileptic used	Drop down menu – see (d) below	*Levetiracetam*
Duration of use of second antiepileptic	Drop down menu – see (e) below	*6 days*
Third Antiepileptic used	Drop down menu – see (d) below	*Topiramate*
Duration of use of third antiepileptic	Drop down menu – see (e) below	*Still being treated with this drug*
Fourth Antiepileptic used	Drop down menu – see (d) below	*Phenobarbital*
Duration of use of fourth antiepileptic	Drop down menu – see (e) below	*3 days*
Fifth Antiepileptic used	Drop down menu – see (d) below	*None*
Duration of use of fifth antiepileptic	Drop down menu – see (e) below	
SCREEN 4 – OTHER THERAPIES		
Since last report, please specify other therapies used		
First other therapy used	Drop down menu – see (f) below	*Steroids*
Duration of use of first other therapy	Drop down menu – see (g) below	*5 days*
Second other therapy used	Drop down menu – see (f) below	*ECT*
Duration of use of second antiepileptic	Drop down menu – see (g) below	*on-off therapy*
Third other therapy used	Drop down menu –	*none*

	see (f) below	
Duration of use of third other therapy	Drop down menu – see (g) below	
Fourth other therapy used	Drop down menu – see (f) below	*none*
Duration of use of fourth other therapy	Drop down menu – see (g) below	

DROP DOWN MENUS

a	- Continuing intensive therapy* - Recovered from status epilepticus and receiving maintenance therapy only** - Therapy withdrawn** - Died*** - I am no longer aware of his therapy***

* Send next follow up questionnaire in 2 weeks
** Send questionnaire 3 (outcome) immediately
*** Do not send any more questionnaires

b	Propofol Thiopental Pentobarbital Midazolam Ketamine Inhalational anaesthetics (specify – free text box) Other (specify – free text box) Don't know

c	Still being treated with this drug 24 hours or less 1-7 days 8-14 days More than 14 days (specify – free text box) Other (specify – free text box) Don't know

d	Phenytoin Phenobarbital Valproate Levetiracetam Carbamazepine

	Clonazepam Clobazam Other benzodiazepine (specify – free text box) Topiramate Lamotrigine Oxcarbazepine Pregabalin Gabapentin Zonisamide Lacosamide Retigabine Perampenil Vigabatrin Other (specify – free text box) None Don't know

e	Still being treated with this drugs 24 hours or less 1 day 2 days 3 days 4 days 5 days 6 days 7 days 8-14 days More than 14 days Other (specify – free text box) Not known

f	Hypothermia Neurosurgery (specify type – free text box) Steroids IVIg Plasma exchange Ketogenic diet Electroconvulsive therapy (ECT), course of Vagal nerve stimulation (VNS) Transcranial magnetic stimulation (TMS). course of Other (specify – free text box) None Don't know

g	Still being treated with this therapy

Version: 1
Date: 1th August 2014

	On-off therapy 24 hours or less 1-7 days 8-14 days More than 14 days (specify – free text box) Other (specify – free text box) Don't know

QUESTIONNAIRE 2 - short version - 2 weeks follow up

What is the current status of therapy, as far as you are aware	Drop down menu (a)	*Patient died*
Are there any amendments or changes to this information ? please specify	Free text box	*Cause of status shown to be stroke not encephalitis*
Did the patient receive any further therapies since last report (anaesthetics, antiepileptics or other..)	Free text box	*None*

Version: 1
Date: 1th August 2014

QUESTIONNAIRE 3 - OUTCOME AT TIME OF DISCHARGE FROM ITU OR DEATH

Question	Format	Example
SCREEN 1		
Is the patient dead or alive	Drop down menu (a)	*Alive*
Duration of stay in ITU (alive /dead at end of ITU stay)	Drop down menu (b)	*10 days*
Outcome on termination of anaesthesia	Drop down menu (c)	*Rankin score 3*
Was active treatment withdrawn	Drop down menu (d)	*No*

QUESTIONAIRE 4 - 3 and 6 month outcome

Question	Format	Example
SCREEN 1		
Longer term outcome if known	Drop down menu (c)	*Rankin score 2*

DROP DOWN MENUS

a	Alive Dead Not known

b	Number of days (please specify) Not known Other (please specify)

c	0 - No symptoms. 1 - No significant disability. Able to carry out all usual activities, despite some symptoms. 2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities. 3 - Moderate disability. Requires some help, but able to walk unassisted. 4 - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted. 5 - Severe disability. Requires constant nursing care and attention, bedridden, incontinent.

	6 - Dead. Not known

d	Yes No Not known Other (please specify)