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Adult/Young Adolescent Information Sheet for STOP'EM

- You have been invited to take part in a research study. Before you decide, it is important that you understand why the research is being done and what it will involve.
- Please take time to read the following information. **Part 1** tells you the purpose of the study and what will happen to you if you take part. **Part 2** gives you more detailed information about the conduct of the study.
- You can ask a member of your clinical team if there is anything that is not clear, or if you would like more information.
- If you wish you can discuss it with friends, relatives and/or get independent advice via your local Patient Advice and Liaison Service (PALS) or equivalent.
- Taking part is voluntary. If you don't want to take part then you don't need to give a reason.
- STOP'EM is a study that will look at whether taking an anti-epileptic drug before surgery prevents seizures happening after surgery.
- The study will compare an anti-epileptic drug called levetiracetam against a placebo.
- To be able to take part you will have been diagnosed with a meningioma brain tumour that needs surgical removal. You will not have had a seizure before and you will be aged 16 years or over.
- The study will recruit 1004 patients across the UK and Ireland, who will be regularly followed-up for 12 months.

How to contact the study team:

If you have any questions about this study please talk to your research team:

- **Principal Investigator:** PI NAME
- **Research Nurse:** RN NAME
- **Telephone:** CONTACT NUMBER

Contents:

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PART 1: Purpose of the study and what will happen if you take part

Why are we doing the STOP'EM study?

Meningioma is the most common primary brain tumour with 5 out of every 100,000 patients a year in the UK receiving this diagnosis. They grow from the lining of the brain. In the UK each year, about 1600 people with a meningioma have surgery to remove the tumour. Approximately 70% of these people will not have had epileptic seizures, but after surgical removal, around 12% will have a seizure within 12 months.

In patients who have never had a seizure, neurosurgeons do not know whether giving an anti-epileptic drug (AED) before surgery (known as prophylaxis) will prevent seizures. Around the world, some neurosurgeons use prophylaxis and others do not.

STOP'EM will compare a well-established AED called levetiracetam, to a placebo (a capsule that looks the same but contains no active drug).

The study will aim to find out whether a 2-week course of levetiracetam, starting shortly before surgery, reduces the risk of developing seizures within 12 months of surgery, compared to 2 weeks of placebo.

Adults aged 16 years or older, who have a meningioma that needs surgical removal and who have not had a seizure before can take part. STOP'EM will recruit 1004 patients. Half of the patients will be given levetiracetam and half will receive placebo.

Patients will follow the normal care pathway and will be followed-up regularly for 12 months to assess if they develop seizures.

The results from this study will be used to help us improve treatments for patients with meningioma that requires surgical removal.

Why have I been invited to take part?

You have been chosen as you have been diagnosed with meningioma and have agreed to have surgery, you are over 16 years of age and have never had a seizure before.

Do I have to take part?

No, taking part is voluntary. It is up to you to decide whether or not you want to take part.

If you decide not to take part then you will still receive the usual treatment your hospital offers. Your doctor can provide you with more information on this.

If you decide to take part you can also choose to stop at any time without giving a reason.

The decision you make on whether to take part or not will not affect the care, or the standard of care you receive now or in the future.

What will happen to me if I take part?

If you agree to take part, you will be asked to sign a consent form. You will be given a copy of the consent form and this information sheet to keep.

Once you have signed the consent form, we will check and confirm that this study is suitable for you and you will be asked to follow the study plan (see study timeline).

We will review your medical history, including any medications you take. We will ask about your ability to perform certain daily activities. You will complete two questionnaires – one will ask about your quality of life, and the other will ask about your use of NHS resources (for example, have you visited your GP or a walk-in centre recently). We will also ask you if you have a driving licence and if you are able to drive.

You will start taking the study treatment, levetiracetam or placebo, 1 day before the meningioma surgery, and will continue to take the treatment for a total of 2 weeks.

If you are happy to provide optional blood samples, we will take 5 in total (about 2 teaspoons per sample). The first will be taken at the start of your surgery, and the others shortly after.

You will have 5 follow-up visits after your surgery. The timing of visits and what will happen is shown in the diagram below.

At each of these follow-up visits, a Research Nurse will ask you about symptoms of a possible seizure. To help you

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understand symptoms of seizures, you will be provided with a contact card that lists some symptoms to look for.

If you develop any of these symptoms, you should contact your local medical team – contact details will be on the card. The team will assess you to determine if you did have a seizure, and the normal care pathway will be followed.

If you experience a seizure in the first 2 weeks after your surgery, your medical team will decide on the next steps to take.

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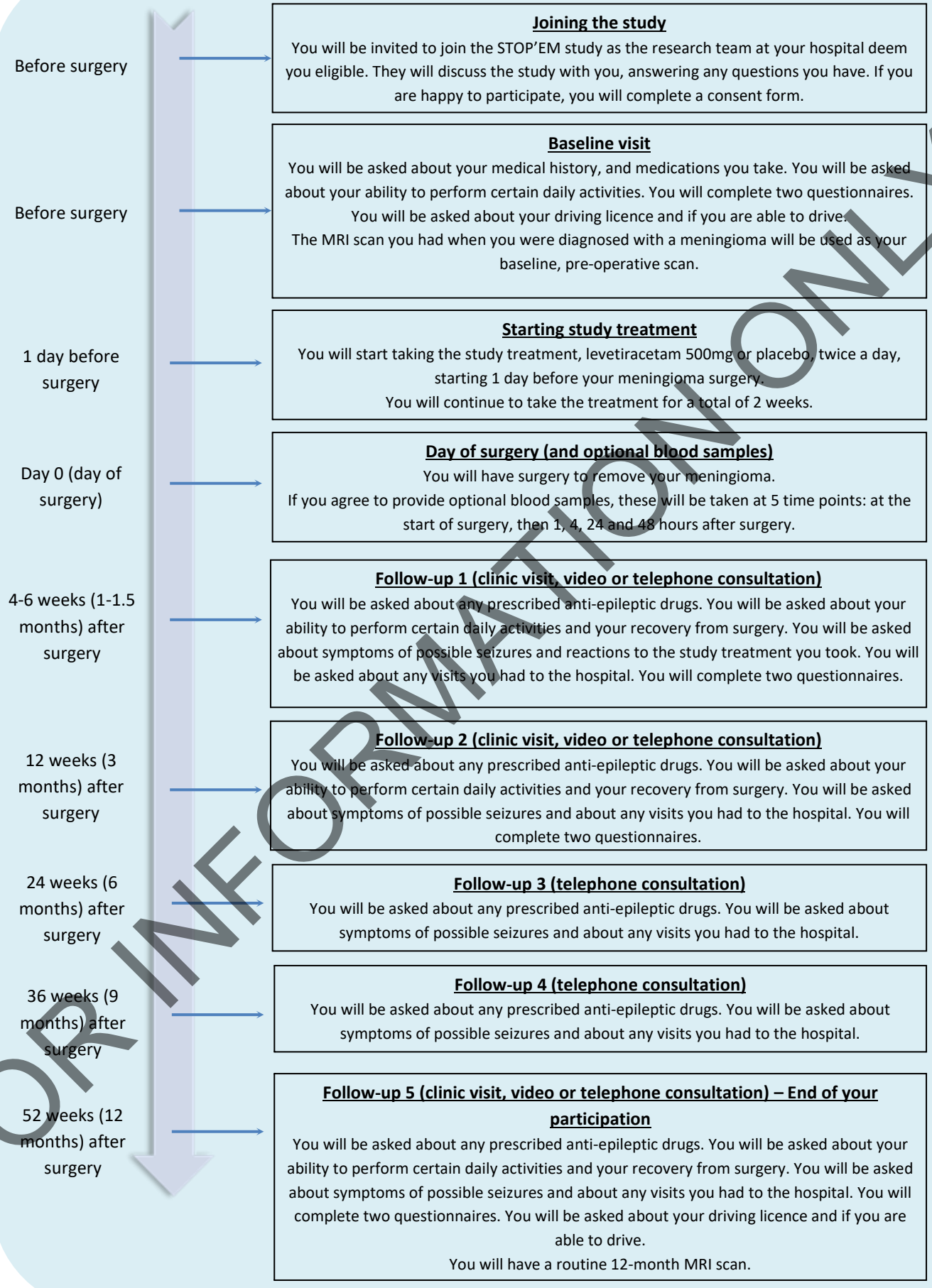

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Procedure	Description	Research Treatment or Standard of care
MRI scan	You will attend hospital for an MRI scan that will help diagnose you with a meningioma. 12 months after you have surgery to remove the meningioma, you will attend hospital and have another MRI scan.	**Standard of Care**
Study treatment (levetiracetam 500mg or placebo)	After you have consented to join the study and had your baseline visit, you will receive your study treatment – you will need to come in to the hospital to receive this. You will be given capsules divided into two bottles: - 1 bottle will contain 2 days' worth of treatment (for use one day before surgery, and on the day of surgery) - 1 bottle will contain 12 days' worth of capsules for you to take after surgery Both bottles will be given to you in a labelled carton. You will take 2 capsules orally, twice a day (morning and evening), for a total of 14 days.	**Research Treatment**
Questionnaires	You will complete two questionnaires – one will ask about your quality of life, and the other will ask about your use of NHS resources. You will complete questionnaires on four occasions: - Before surgery (at your baseline visit) - 4-6 weeks (1-1.5 months) after surgery (at follow-up 1) - 12 weeks (3 months) after surgery (at follow-up 2) - 52 weeks (12 months) after surgery (at follow-up 5, which will be the end of your participation) Your questionnaire responses will be reviewed by your local medical team. They will discuss with you if other support services are needed.	**Research Treatment**
Blood samples (optional)	If you consent to provide blood samples, 5 will be taken in total: - At the start of surgery - 1 hour after surgery - 4 hours after surgery - 24 hours after surgery - 48 hours after surgery	**Research Treatment**

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What is the drug being tested?

Levetiracetam is a well-established anti-epileptic drug used to treat people who have epileptic seizures. It is being compared to a placebo (this capsule will look the same as levetiracetam, but has no active drug inside and is perfectly safe for consumption).

You will take 2 capsules orally (by mouth), twice a day (morning and evening), for a total of 14 days. If you take levetiracetam, each capsule contains 250mg of the drug.

The capsules have a gelatin coating. We will ask you to take the capsules at approximately the same time each day, spaced as close to 12 hours apart as possible.

The first two doses will be taken in the 24 hours before your surgery to remove the meningioma.

Will I know which treatment I'm going to have?

This study is a type of trial called a 'blinded trial' which means that neither you nor the research team will know which treatment you will be receiving.

In research studies we split patients up into groups to look at how different treatments work. In the STOP'EM study patients will be split into two treatment groups at random:

- One group will receive 500mg (2 x 250mg capsules) levetiracetam, twice a day
- The other group will receive placebo, twice a day

It is really important that each group in the STOP'EM study has a similar mix of patients in it. If there is a difference in seizures between the two groups, then we will know that this is due to the treatment (i.e. the levetiracetam) and not because there are differences in the types of patients in each group.

We use a computer programme that puts patients into groups 'at random' – you might hear this described as 'randomisation' or 'random allocation', but they all mean the same thing. Neither you nor your doctor choose which group you are in.

In the STOP'EM study you are equally as likely to be in the group receiving levetiracetam as you are in the group receiving placebo. So, you and your medical team will not know which treatment you will have.

At the end of the study, if you wish to know which treatment group you were in, you can ask your study team and they can tell you.

What are the alternatives for treatment?

If you have been approached for this study, it is because you have not had seizures before. After surgery, if you do begin experiencing seizures, you may be prescribed an anti-epileptic drug. Levetiracetam, the drug being tested in this study, may be prescribed for you, as this is commonly used. However, there are other anti-epileptic drugs you could also be prescribed.

What are the benefits and risks of taking part?

Possible common side effects when people take levetiracetam are:

- Drowsiness
- Headache
- Fatigue
- Dizziness

Please contact your study team if you experience any of these symptoms. The contact telephone number(s) can be found on page 1 of this Information Sheet.

We hope that the results from the study will help patients and doctors in the future when making decisions about treatment.

What happens if I change my mind?

If at any point you decide to stop taking part in the study you will still receive standard treatment and follow up usually offered by your hospital.

If you do decide to stop taking part we will ask you if you would like to:

- continue to complete follow up visits for the study **or**
- stop taking part with no more study visits.

Information on how we will handle your information and samples in the event of you withdrawing is detailed in Part 2 of this Information Sheet.

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What if new information becomes available?

Sometimes during the course of a research project, important new information becomes available about the drug that is being studied. As the treatment course in STOP'EM is short we do not anticipate that any new information will become available that will impact your ongoing participation in the study. However, if this does happen, your doctor will tell you about it and you may be asked to sign an updated consent form should you decide to continue in the study. If you decide to withdraw from the study, your doctor will arrange for your care to continue.

On receiving new information your doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue.

If the study is stopped for any other reason you will be told why and your continuing care will be arranged.

What happens when the study stops?

Once you have had the 52 weeks (12 months) study visit no further study visits are required. You will continue to have follow-up with your medical team for the meningioma. Your medical team can provide details on whether you need more MRI scans or clinic visits.

It is intended that the results of the study will be presented at conferences and published in medical journals so that we can explain to the medical community what our research results have shown. They may also be used to apply to the regulatory authorities to make the drug widely available and/or for research related to the development of pharmaceutical products, diagnostics or medical aids. Confidentiality will be ensured at all times and you will not be identified in any publication.

Any information derived directly or indirectly from this research, as well as any patents, diagnostic tests, drugs, or biological products developed directly or indirectly as a result of this research may be used for commercial purposes. You have no right to this property or to any share of the profits that may be earned directly or indirectly as a result of this research. However, in signing this form and donating MRI images and/or blood samples for this research, you do not give up any rights that you would otherwise have as a participant in research.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Detailed information is given in Part 2 of this information sheet.

Will my taking part in the study be kept confidential?

Yes. All the confidential information about your participation in this study will be kept confidential. Detailed information on this is given in Part 2.

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PART 2: Detailed Information about the conduct of the study

Who is running the study?

University of Liverpool is the Sponsor of this study and is responsible for managing it. They are based in United Kingdom. They have asked that the day to day running of the study is carried out by a team based at the Liverpool Clinical Trials Centre (LCTC, part of the University of Liverpool), health economics researchers from Bangor University (the central study team), the Neuroimaging team at The Walton Centre NHS Foundation Trust (Liverpool), and the laboratory team at Cambridge Neurosurgical Laboratories (Addenbrooke's Hospital, Cambridge).

The study has been reviewed by the Medicines and Healthcare Products Regulatory Agency, the Health Research Authority and the National Research Ethics Service Committee to make sure that the study is scientifically and ethically acceptable.

This study is funded by National Institute for Health Research (NIHR) Health Technology Assessment programme (HTA) (NIHR Reference: NIHR129748).

Your doctor will not receive any personal payment for including you in this study. The hospital may receive additional funding to help with any extra costs that supporting this study might incur.

How will my information be collected and handled?

University of Liverpool and Bangor University are the Data Controllers for this study and will need to use information from you and your medical records for this research project.

This information will include your study ID number, initials, date of birth, NHS number (England only) and postcode (England only). People will use this information to do the research or to check your records to make sure that the research is being done properly.

Individuals from University of Liverpool, the LCTC, Bangor University, The Walton Centre NHS Foundation Trust, Cambridge Neurosurgical Laboratories, and regulatory organisations may look at your medical and research records to check the accuracy of the research study.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

Data will be sent from your hospital to the LCTC – the study team at your hospital will enter data onto a secure database that LCTC can see.

Data relating to the questionnaires you complete will be sent from LCTC to Bangor University. Your personal details (name, postcode, date of birth, NHS number and study ID number) will be shared with NHS Digital (for England only) by LCTC in order for them to provide information already in their possession on your hospital attendances for the financial years commencing 6 months before the start of the study and covering the duration of the study. NHS Digital (England only) will then share this health information, which is regarded as a special category of information, with relevant members of the research team at Bangor University. The data provided will have removed your name, date of birth and other identifiers. At the end of the period specified in the NHS Digital Data Sharing Agreement, the data provided will be securely destroyed.

If you are in a hospital site in Scotland or Wales, the Health Economics team working at Bangor University will request information on your hospital appointments directly from your NHS hospital. Bangor University will not receive any identifiable information about you.

Your MRI scans and data relating to these will be sent from your hospital to the Neuroimaging team at The Walton Centre NHS Foundation Trust (Liverpool).

Data relating to optional blood samples will be sent from your hospital to the laboratory team at Cambridge Neurosurgical Laboratories (Addenbrooke's Hospital, Cambridge).

We will notify your GP that you will be taking part in the study for their information.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep the data for 15 years, so we can check the results. We will write

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our reports in a way that no-one can work out that you took part in the study.

What are my choices about how my information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from your hospital. If you do not want this to happen, tell us and we will stop.

In some cases however we may need to continue to collect limited information about any side-effects of the study treatment you may experience. We will only do this where we are required to do so by law.

We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

Information sharing for other research

When you agree to take part in a research study, the information about your health and care may be beneficial to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad. Your information will only be used by organisations and researchers to conduct research in accordance with the UK Policy Framework for Health and Social Care Research, or equivalent standards.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can I find out more about how my information is used?

You can find out more about how we use your information:

- at the LCTC website: https://lctc.org.uk/privacy
- at www.hra.nhs.uk/information-about-patients
- by asking one of the research team
- in the Health Research Authority leaflet available from www.hra.nhs.uk/patientdataandresearch
- by contacting the University of Liverpool Data Protection Officer on LegalServices@liverpool.ac.uk
- in the LCTC's "Privacy Notice" available from: https://www.lctc.org.uk/privacy
- by contacting the University of Bangor Data Protection Officer at gwenan.hine@bangor.ac.uk
- at Bangor University's website: https://cheme.bangor.ac.uk/data-protection.php.en

If you are not happy with the way your information is being handled, or with the response received from us, you have the right to lodge a complaint with the Information Commissioner's Office at Wycliffe House, Water Lane, Wilmslow, SK9 5AF (www.ico.org.uk).

What will happen to the blood samples I give?

If your centre is taking part in STOP'EM blood sample collection, they will discuss this optional part of the study with you.

With your permission, we would like to collect 5 blood samples so they can be stored for a future research study to investigate whether blood markers (biomarkers) can be used to predict which patients will have seizures after surgery.

This will require us to collect a large number of samples before we can carry out any analysis. We would like to collect 5 blood samples from everyone who consents (about 2 teaspoons of blood per sample).

We hope that, in the future, these biomarkers can be used to more accurately advise patients as to what their seizure risk is, and whether they should take an anti-epileptic drug, like levetiracetam, or not.

If you agree to give blood samples, we will ask you to sign a separate consent form. Coded samples will be sent to Cambridge Neurosurgical Laboratories, Level 6, A-block, Addenbrooke's Hospital, Hills Road, Cambridge for storage. Some of the data we collect about you in this study will be provided alongside your samples – this too will be coded. These researchers work closely with other scientists in the UK and elsewhere and may transfer your samples to these research collaborators for use in future

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scientific studies. Your samples will not be transferred outside of the UK.

These samples may be used for genetic testing for specific biomarkers of inflammation that can have an effect on seizure risk.

The samples will be kept in a secure place until we need them; nobody outside of the study will have access to **any** confidential information that you give to us. Confidential details (such as your address and GP details) will be kept locally and not made available to collaborators.

Separate funding and approval will be sought for any future research that involves your samples.

If you choose to withdraw from the study, we won't collect any more samples from you, but we will continue to store the samples we have already collected and these will be made available to future researchers. If you do not want us to do this, please let us know and we will stop where possible. It may however not be possible to stop this where the samples have already been provided to researchers.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with one of your research team who will do their best to answer your questions.

If you remain unhappy and wish to complain formally, you can do this by contacting local NHS Patient Advice and Liaison Service (PALS) or equivalent. Members of your local hospital team should be able to provide this information to you.

Every care will be taken of you in the course of this clinical study. However, in the unlikely event that you are harmed by taking part in this research project of the study Sponsor (University of Liverpool), compensation may be available and you may have to pay your related legal costs. Your hospital where you receive your treatment has a duty of care to you whether or not you agree to participate in the study and the study Sponsor accepts no liability for negligence on the part of your hospital's employees. However, if you are harmed and this is due to someone's negligence at the hospital, then you may have grounds for a legal action for compensation against the NHS Trust where you are being treated but you may have to pay for your legal costs. The normal National Health Service complaints procedures should be available to you.

Thank you for taking the time to read and consider this information sheet. Should you decide to take part in the study, you will be given a copy of the information sheet and a signed consent form to keep.

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FOR SITE USE ONLY:

Site Name:																			
Participant Screening No.:																			
Participant Initials:				Participant DOB:			/			/									

Adult/Young Adolescent Consent Form

To be completed by the participant:

Once you have read and understood each statement please enter your initials in each box.	Initial
1. I have read and understood the information sheet for this study. I have had the opportunity to ask questions and have had these answered satisfactorily.	
2. I understand that participation is voluntary and that I am free to withdraw from the study at any time, without giving a reason, and without my care or legal rights being affected. However, the study team may need to collect some limited information for safety reasons.	
3. I agree to take part in the above study.	
4. I give permission for a copy of this fully completed consent form to be sent to the LCTC (where it will be kept in a secure location) to allow confirmation that my consent was given.	
5. I understand that relevant sections of my medical notes and any data collected during the study may be looked at by authorised individuals from the central study team and representatives of the Sponsor, regulatory authorities and the local NHS Trust. I give permission for these individuals to have access to my records and data.	
6. I agree to my GP being informed of my participation in the study.	
7. I agree for the relevant data on my NHS hospital admissions and treatment to be collected for the purposes of this study and understand this will involve accessing data from my hospital's finance office.	
8. I agree for the relevant data on my NHS hospital admissions and treatment to be collected for the purposes of this study and understand this will include accessing electronic NHS health care records from NHS Digital (England) for the financial years commencing 6 months before the start of the study and covering the duration of the study, for health economic analysis **(for England only)**.	
9. I agree for my personal data (including name, postcode, date of birth, NHS number) to be shared with NHS Digital (England) so they can provide Health Economic researchers working on the study with information regarding my medical data and hospital attendances **(for England only)**.	
10. I agree for my medical data held by NHS Digital (England) to be obtained by Bangor University for use on this study **(for England only)**.	
11. I understand that my data will be kept by the University of Liverpool, Bangor University, The Walton Centre NHS Foundation Trust, Cambridge Neurosurgical Laboratories, and at my hospital in a confidential manner for 15 years from the end of the study.	

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Postcode:					-					

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FOR SITE USE ONLY:

Site Name:																					
Participant Screening No.:																					
Participant Initials:				Participant DOB:			/			/											

Adult/Young Adolescent Consent Form

The statements below are optional (you can still take part in the study even if you do not wish to agree to these): Please enter your initials in each box if you agree to the statements below. **If you do not agree, please leave blank**.

12. I agree to allow information and data or results arising from this study to be used in future healthcare and/or medical research providing my confidentiality is maintained. ☐

13. I agree that I may be contacted in the future in relation to this or other related studies. ☐
(if you agree to this statement provide your details below):

Telephone number:	
Email address:	

To be completed by the participant:

Your full name (please print):			
Your signature:		Date:	

To be completed by the Researcher (after participant has completed the form):

Researcher full name (please print):			
Researcher signature:		Date:	

Please make two copies: one for the participant and one for the medical notes. Please upload a scanned copy to REDCap for LCTC. Please file the original wet-ink copy in the STOP'EM Investigator Site File.

To be completed by the Translator (if used):

Translator full name (please print):			
Translator signature:		Date:	

To be completed by the Impartial Witness (if used):

Witness full name (please print):			
Witness signature:		Date:	
Participant's full name (please print):			

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