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Participant Information Sheet (PIS)

Artificial intelligence-assisted magnetic resonance imaging for quality, efficiency and equity in the NHS care of multiple sclerosis (AssistMS)

Invitation and summary

You are invited to join the AssistMS study because you have been diagnosed with Multiple Sclerosis (MS) or a condition called Clinically Isolated Syndrome (CIS) that suggests you may have MS.
MS is a long-term disease that affects over 150,000 people in the UK. Starting treatment early is important for managing MS. It's also essential to monitor your treatment to see if it's working and to switch treatments if needed.

In practice, magnetic resonance imaging (MRI) is the only accepted tool to monitor how well your treatment is working. However, visually detecting subtle changes on MRI scans is time-consuming and tiring for the radiologists and therefore they may make mistakes.

In this study, we are testing an Artificial Intelligence (AI) software called "ico**brain ms**." developed by the company “ico**metrix**” (Leuven, Belgium). This tool helps track MS by measuring changes in the brain using MRI scans. The AI can highlight problem areas and create reports that doctors can use to make better decisions about your treatment. With this study, we hope to prove that ico**brain ms** can be used to assist the neuro-radiologist with their visual assessment of MRI scans by a radiologist, and that it will help clinicians make more informed decisions about your current MS treatment.

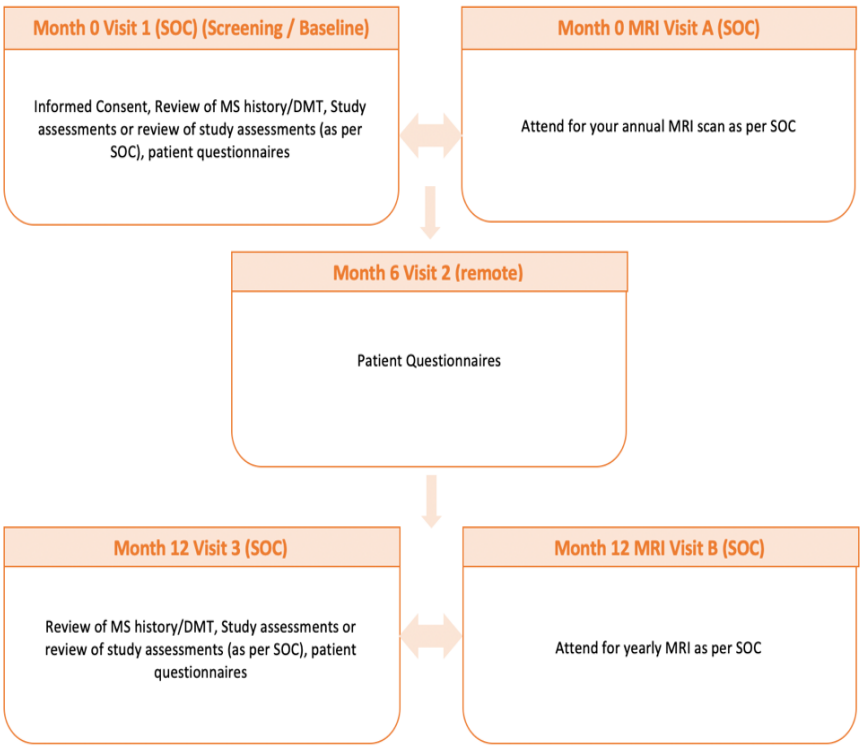
Taking part in this study is entirely up to you, and your MS care will not be affected if you choose not to participate.

Purpose of and background to the research and invitation

Without the right treatment, many people with MS can develop significant disabilities within 10 years of diagnosis. The main challenge in treating MS is to find a treatment that reduces disease activity, preventing brain damage and worsening disabilities.
Currently, brain MRI scans are evaluated visually by radiologists. This method can miss important details due to factors like time constraints, fatigue, and differences in MRI techniques and equipment across hospitals. Our goal is to prove that using this assistive AI tool can improve the accuracy of MRI evaluations. Research shows that detecting new lesions can be 3-4 times higher with assistive software compared to visual inspection alone.
The AI software used in this study, ico**brain ms** has been tested and licensed through multiple international studies. Previous research suggests that this tool can improve decision-making, quality, speed, and consistency in healthcare. However, its impact in NHS practice is still uncertain and needs further evaluation. We hope that using ico**brain ms** will enhance the quality and speed of MRI scan assessments, leading to faster treatment decisions, better patient outcomes, and reduced healthcare costs.

Do I have to take part in the study?

Taking part in this study is entirely up to you. If you decide not to participate, it won't affect your medical care. If you do choose to participate, you can leave the study at any time without needing to provide a reason.



What would taking part involve?

About 1,336 people with MS will take part in this UK-wide study. If you agree to participate, you will be in the study for about 12-15 months, including any follow-up visits that are already part of your regular care.

If you decide to join, you won't need to do anything new besides attending your scheduled MS clinic visits, having your regular MRI scans, and completing a few online questionnaires we will send you. Additionally, we ask that you:

- Inform your doctor about any changes in your health, medications, or hospital visits, including admissions, since your last appointment.
- Let your doctor know if you participate in any other research study.
- Notify your doctor if you change your mind about participating in this study; you can leave the study at any time without any negative impact on your medical care.

If you agree to participate, you will need to sign the Informed Consent and you will then receive a copy. Only after that will specific data from your medical records be collected and analysed as part of the study.

Analysis of Your MRI Scans

Your MRI scans can be analysed in two ways during this study:

1. Usual method: your neuro-radiologist visually inspects the scans, following routine clinical practice.
2. Your neuro-radiologist visually inspects the scans with ico**brain ms** to assist in the analysis.

The choice between these two methods will be random, meaning neither you, your doctor, nor your radiologist can decide which method is used. At your regular visits, your doctor will discuss the results with you and explain what they mean for your MS care.

If your MRI scans are analysed using ico**brain ms**, only the following information will be included:

- Year of birth

- Sex at birth (M/F)
- Assigned trial number

This ensures that no personal details, such as your name, NHS/hospital number, address, or email, will be shared with ico**metrix**. Additionally, the main dataset of the trial will not contain any personal data, no matter which group you are in.

Sub-study: Analysis by Non-Expert Radiologists

A small part of this study, called a sub-study, involves general radiologists (who are not neuro-radiologists) reviewing a selection of MRI scans. These scans may include yours and will be chosen randomly. Like in the main study, these radiologists will not know who the scans belong to and will only have the same basic information attached (year of birth, sex at birth, and trial number). The goal of this sub-study is to compare the analysis of general radiologists with that of specialist neuro-radiologists. However, their findings will not affect the main study.

What Happens If You Decide to Take Part?

If you decide to take part, a member of the clinical care team will talk to you during one of your routine hospital or telephone appointments. They can explain the study in more detail and answer any questions you might have. You'll also be given a weblink where you can register your interest in the study and download a patient information sheet for more details.

You will have as much time as you need to think about whether you want to join the trial. You should have at least one day to review the trial information before being asked to consent.

If you agree to take part, the next time you attend a routine appointment or MRI, you'll be asked to review the Patient Information Sheet (PIS) electronically. At that point, if you wish to formally review the consent form with a health care professional (HCP) this can be done either at the hospital during your routine visit or remotely with a secure video link. The video will not be recorded and is only to provide a convenient option for the discussion. Then, you will electronically or normally sign a consent form to confirm that you understand the information and are willing to participate. You'll receive a copy of your signed consent form, either as a hard copy or a PDF sent to your email.

However, giving your consent doesn't automatically guarantee your participation. Your doctor or nurse will go over the consent form with you to make sure you fully understand the study and any potential risks.

At your first visit with the clinical trial team (screening/baseline visit), the following information will be collected and entered into the trial database. This data will be grouped using your unique trial number, so no information that could identify you personally will be included.

- Your date of birth
- Sex at birth (M/F)
- Gender
- Ethnic group

The following MS specific related information will be collected:

- MS type (Relapsing Remitting MS, Secondary Progressive MS, Primary Progressive MS or Clinically Isolated Syndrome (CIS))
- Year of MS Diagnosis
- Age at MS Diagnosis
- Current Disease Modifying Therapy (DMT) (if applicable)
- Most recent past MRI of your head (if applicable)
- Most recent Expanded Disability Status Scale (EDSS, done by doctor and nurse)) or web-EDSS (done by yourself)
- Most recent Nine Hole Peg Test (9-HPT) results (if this is part of your standard of care and only if available)
- Most recent Timed 25 Foot Walk (T25FW) results (if this is part of your standard of care and only if available)
- Most recent Symbol Digit Modality Test (SDMT) and/or Symbol Substitution task (SST) results (if this is part of your standard of care and only if available)
- Most recent Neurofilament Light Chain test (cerebral spinal fluid (CSF) or blood serum) results ((if this is part of your standard of care and only if available)
- EQ-5D-5L (ePRO questionnaire filled in by you)
- Healthcare and Other Resource Use Questionnaire (ePRO questionnaire filled in by you)
- Relapse Review
- DMT Review

<u>Month 0 (MRI Visit A)</u>

- Attend for annual MRI as per standard of care (this visit could be before or after your screening/baseline visit discussed above.

<u>Month 6 ((Remote) Visit 2):</u>

- Euroqol EQ-5D-5L (ePRO questionnaire filled in by you)
- Healthcare and Other Resource Use Questionnaire (ePRO questionnaire filled in by you)

Month 12 (Visit 3):

- web-EDSS or clinical EDSS (EDSS, done by doctor and nurse)) or web-EDSS (done by yourself)
- 9HPT (if this is part of your standard of care and only if available)
- T25fWT (if this is part of your standard of care and only if available)
- SDMT and/or Symbol Substitution task (SST) (if this is part of your standard of care and only if available)
- Cerebral Spinal Fluid (CSF) or serum (s) Neurofilament light level (cNfL/sNfL) (if this is part of your standard of care and only if available)
- EQ-5D-5L (ePRO questionnaire filled in by you)
- Healthcare and Other Resource Use Questionnaire (ePRO questionnaire filled in by you)
- Relapse Review
- DMT Review
- DARS datasets (Optional and information supplied by your clinical team)

Month 12 (Visit B):

- Attend for yearly MRI as per standard of care

AssistMS Assessments Schedule					
Study Procedures	**Visit 1 (Screening and Baseline during SOC visit) (also M0 MRI visit A)**	**Visit 2 (ePROs only)**	**Visit 3 (End of trial during SOC visit) (also M12 MRI visit B)**	**Early Withdrawal**	**Unscheduled Visit**
	(+/-12 weeks to Day 0 from baseline visit at Visit A) (M0 MRI visit)	**M6 (+/- 2 weeks)**	**M12 (+/- 12 weeks)**		
Review and Sign Consent Form	x				
Review of your MS Medical History, MS DMT Drug History and demographic data	x				
Check if you are eligible for the trial (inclusion and exclusion criteria)	x				
As part of your SOC, you will be asked to complete the web-EDSS or your clinical team will perform the EDSS with you	x		x	(X)	x
Result of the 9HPT (if you have done one)	(x)		(x)	(x)	(x)
Result of the T25FW test (if you have done one)	(x)		(x)	(x)	(x)
Result of the SDMT and/or SST (if you have done one)	(x)		(x)	(x)	(x)
Result of neurofilament light chain level (CSF or blood serum) (if you have done one)	(x)		(x)	(x)	(x)

You will be asked to complete the EQ-5D-5L questionnaire (electronic)	x	x	x		x
You will be asked to complete the Health Resource Use Questionnaire (electronic)	x	x	x		x
Your doctor will check to see if you have had a relapse	x		x	(x)	x
Review of your current MS DMT medication	x		x	(x)	x
DARS datasets (optional)			x		
MRI scan (as SoC-at any point 12 weeks before or after your annual clinic visit)	x		x		(x)
Abbreviations	SoC = Standard of Care, M0 = Month 0, M6 = Month 6, M12 = Month 12, MS = Multiple Sclerosis, MRI = Magnetic Resonance Imaging, DMT = Disease Modifying Therapy, EDSS = Expanded Disability Status Scale, 9HPT = Nine-Hole Peg Test, T25fW = Timed-25 Foot walk, SDMT = Symbol Digit Modality Test, CSF = Cerebrospinal Fluid, DARS = Data Access Request Service; (X)=only if available				

Collection of Personal Data and What Will Happen with This Information
During your visits with the clinical trial team, they will collect your information and enter it into a trial database using a unique trial number. This means your identity won't be linked to the information in the database.

For this research, we'll use data from you, your hospital records, and, optionally, national NHS databases. Only people who need to see this information will have access to it. Others will only see your data as a study ID number, not your name or contact details. This is called pseudonymised data. We'll keep your information secure. Your pseudonymised MRI data will be stored on a cloud based server in Ireland, with a backup in Germany, for the duration of the study and for 25 years after that.

If you lose the ability to make healthcare decisions during the study, no extra tests will be done for research, but we will continue to use information gathered from your regular care.
After the study, some data will be kept to verify the results, but we'll write our reports in a way that doesn't reveal your identity. Your study data will be stored for up to 25 years and then securely destroyed.

If you participate, we'll inform your GP. Your medical records might be reviewed by the research team, the sponsor, regulatory authorities, and authorised sponsor representatives to make sure the trial is conducted correctly. If you change your GP during the study, please let the study team know as soon as possible.

Where can you find out more about how your information is used? You can find more information on how your data is used at www.hra.nhs.uk/information-about-patients/ , by asking one of the research team or by emailing assistms@qmul.ac.uk or QMUL's data protection officer at data-protection@qmul.ac.uk.

This part of the study is optional:

To identify larger trends in the study, we may access certain NHS England datasets. We will share limited personal details like your NHS number, birth sex, date of birth, and postcode with appropriate organizations, such as your hospital and NHS England. This is done to link your study data to other NHS relevant organisations and records. The linked data will be temporary and won't include other identifying information. After linking, this temporary data will be destroyed. All data collected during the study follows strict data protection laws.

We might also use these NHS datasets to follow up with you for up to 10 years after the study ends.

What are your choices about your patient data?

- You can leave the study at any time without giving a reason. The research team will keep the data they've already collected from you.
- In some cases, even after this study ends, the research team may collect more information from your doctor or NHS records to track your health. If you don't want this, you can ask to stop further data collection.
- Researchers need to manage your records in a specific way to ensure the research is reliable. This means they can't let you change or remove the data they hold about you, as it could affect the study results.

What Happens to My Research Data After the Study?

Researchers will write reports in a way that no one can tell you were part of the study.

After the study ends, the research team will keep your data for several years to check the results if needed. You can ask who will keep it, whether it includes your name, and how long it will be stored. Your personal details (like your name) will be kept for 25 years after the study ends, so we can send you the research results and contact you about future studies if you've agreed. After 25 years, your personal details will be destroyed.

The hospital where you took part in the study will keep a copy of the research data along with your name. The organization running the research will generally keep a coded version of your data without your name, to check the results.

You may be asked if you want your research data to be used in future studies. This future research might use data without your name or NHS number or may use data that could identify you. You'll be given details about this choice, including whether your data will be linked with other information like your GP or social services records.

Once your name and NHS number are removed, other researchers won't be able to contact you about future research. Any information that could identify you will be stored securely with strict access limits. You might also have the option to allow the hospital or researchers to keep your contact details and some health information to invite you to future studies. Your data won't be used to sell anything to you or shared with other companies except for research purposes.

Will the Use of My Data Meet GDPR Rules?

Yes, your data will be used according to GDPR rules. The UK follows GDPR and the Data Protection Act. All research that uses patient data must follow these rules.

Universities, NHS organizations, and companies can use patient data for research to improve health and care. When companies do research to develop new treatments, they must prove that they need patient data and that it's necessary for the research. This is known as having a "legitimate interest" in using patient data.

Universities and the NHS, funded by taxes, also need to prove that they require patient data for research. This is considered a "task in the public interest." If they can conduct the research without using patient data, they won't be allowed to access your data.

Researchers must consider the views of patients and the public and show how they protect the privacy of participants. An NHS research ethics committee reviews this before the research begins.

All your information will be handled, stored, and destroyed according to GDPR and the Data Protection Act 2018. Data will be kept by the sponsor for 25 years in a pseudonymised way. When shared with other researchers, your data will be fully anonymised.

How Will My Information Be Kept Confidential?

Your health and personal information will be collected and kept confidential throughout the study. This includes:

1. **Medical Record Information**: Held by your [study site.]
2. **Study Data**: Collected during the study but does not contain any personal details that could identify you. This data will be held by the[study site], Queen Mary University of London (QMUL), ico**metrix**, Castor EDC, QMUL affiliates, and representatives.

To ensure your data is kept confidential, your information will be recorded in a way that protects your privacy. However, certain people and organizations will have access to your original medical records to ensure the study is conducted correctly. These include:

- **Authorized Individuals**: Study monitors from QMUL, collaborators, and companies working with QMUL.
- **Regulatory Authorities**: Government agencies that ensure research is safe.

Your study data, which will be labeled with your patient ID or fully anonymised, may be shared with QMUL, ico**metrix**, collaborators, and licensees. Independent researchers or government agencies may also receive your data, but only after personal identifiers have been removed.

Your study data might be combined with data from other people and linked to other information collected from you. It will be used to improve understanding of diseases, assess disease progression, and develop new healthcare solutions. If the study results are published, your identity will remain confidential.

What Will Happen If I Do Not Carry On with the Study?

If you decide to stop participating in the study, we will stop collecting any new data from you. However, we will still use the data that was collected before you withdrew. We will ensure that your personal information is used in the most minimal way possible to protect your privacy, as described earlier.

Does This Affect My Lifestyle?

Your lifestyle should not be affected by the study. All visits will happen during your regular doctor and MRI appointments, except for two questionnaires that you will complete online at the 6-month mark. You will need to keep your doctor informed of any changes in your health, such as new symptoms, medications, hospital visits, or pregnancy, just as you would in your usual medical care.

What Are the Possible Benefits of Taking Part?

There is no direct medical benefit to you from participating in this study. However, if your brain scans are analyzed using ico**brain ms**, it may help your doctor get a better understanding of any changes in your condition, which could lead to more informed decisions about your care. Additionally, the information from this study may help researchers and doctors improve medical care for other people with MS in the future, potentially benefiting you and others down the line.

Possible Disadvantages and Risks of Taking Part

Since this study does not involve a drug or medical device that directly affects you, the risks are primarily related to data:

- **Accidental Identification**: There is a small risk that your MRI data could mistakenly include information that identifies you to ico**metrix**. However, safeguards are in place to ensure this information doesn't go any further, and if it happens, your doctor will inform you and explain what was done to protect your information, including deleting the file.
- **False Positives**: The ico**brain ms** software may incorrectly identify brain lesions or abnormalities. In testing, the software had a 0.3% false detection rate, meaning 3 out of 1,000 scans might have errors. In comparison, according to one study, human neuroradiologists have a 2% error rate (20 out of 1,000), although these mistakes are usually caught during review. Errors in ico**brain ms** might occur due to poor-quality MRI images; however, these scans will be checked and reviewed by neuro-radiologists.
- **Unexpected Findings**: ico**brain ms** may detect brain lesions or abnormalities that standard visual checks might miss. While this is the goal of the study, discovering an undiagnosed or worsening condition could be distressing.

What If New Information Becomes Available?

If new important information about ico**brain ms** arises during the study, we will inform you and ask if you wish to continue participating. If you choose to stay in the study, you might be asked to sign an updated consent form. In some cases, your doctor may feel it's best for you to leave the study based on new information and will discuss this with you.

What If There Is a Problem?

If you have any concerns about the study, please contact your study doctor using the details provided at the end of this information sheet. If you have a complaint, you can reach out to the research team, who will do their best to address your concerns.

You can also contact the Independent Patient Advice and Liaison Service (PALS) at the hospital, whose details are also listed at the end of the information sheet.

If you are harmed as a result of participating in this study, Queen Mary University of London will compensate you, as long as it can be shown that the injury was caused directly by the procedures or interventions you received during the study. This special compensation does not affect your right to seek legal action if necessary.

Expenses and payments?
You will not be paid for your participation in this study as all visits are part of your Standard of Care.

Will I Be Told About New Information?

If there are any new findings during the study that could affect your health or decision to continue participating, your doctor will inform you or your authorized representative as soon as possible. If any of these findings relate specifically to your health, your doctor will discuss them with you, just as they would in regular medical care.

What Will Happen to the Results of This Study?
The results of this study will be summarized in a clinical study report, which will be available to anyone who requests it. Before sharing the report, steps will be taken to ensure that your information cannot be linked back to you. If the study results are published, your identity will remain confidential. If you want to know the results, talk to your healthcare provider, who can arrange for you to receive a summary once they are published.

Future Research

If you're eligible for this study, the investigator may invite you to participate in future research. This is optional, and your choice will not affect the care you receive in this study or as part of your regular treatment. At the end of the study, ico**metrix** will keep an anonymised copy of your data for further research. This data may be used for additional analyses or software development. To protect your privacy, all identifying information will be removed, and MRI images will be altered to ensure anonymity.

Who is Organising and Funding This Study?
This study is funded by the National Institute for Health Research (NIHR) as part of their AI Award for Phase 3: Real-world testing. The AssistMS project is co-led by ico**metrix** (Dr. Jan Verheyden) and Queen Mary University of London (QMUL) (Prof. Klaus Schmierer). Prof. Schmierer is also the Chief Investigator for the AssistMS clinical trial.

How Have Patients and the Public Been Involved in This Study?
AssistMS was created through collaboration between neurologists, image analysts, and patients with multiple sclerosis (MS). This reflects the desire of MS patients to manage their condition safely and effectively. The study's Patient and Public Involvement (PPI) lead, Dominic Shadbolt, has relapsing MS and regularly shares his experiences on his YouTube channel, theMSguide.com. Additionally, Prof. Schmierer has strong connections with the MS Society, UK MS Register, MS Trust, and shift.ms, ensuring that AssistMS remains focused on the needs of people with MS.

Who has reviewed this study?
This study has been reviewed and approved by a Research Ethics Committee (REC), an organisation that is responsible for protecting the rights, safety, and well-being of patients who take part in

research studies as well as the Health Research Authority (HRA). This study has been reviewed and given a favourable opinion by the Dulwich Research Ethics Committee.

Further information and contact details:

If you have any questions, please feel free to ask a member of the research team. Please keep this copy of the AssistMS participant information sheet. If you would like to ask any questions or receive more information about the study, then please contact one of the following:

Research Nurse	***Local investigator***	***Patient Advice and Liaison Service (PALS)***
Name: *Address:* *Number:* *Email:*	*Name:* *Address:* *Number:* *Email:*	*Name:* *Address:* *Number:* *Email:*

Thank you for taking the time to read this information sheet

INFORMED CONSENT FORM

Artificial intelligence-assisted magnetic resonance imaging for quality, efficiency and equity in the NHS care of multiple sclerosis (AssistMS)

Chief Investigator: Prof. Klaus Schmierer

REC Reference number: 24/PR/1584 IRAS ID: 336126

Participant Trial ID	XXX-XXX
Site ID	XXX
Principal Investigator	

Please initial each box to confirm consent		Initials
1.	I confirm that I have read and understood the participant information sheet (PIS) dated 14/Jan/2025, version 2.0 for the above study. I have had the opportunity to consider the information, ask questions about the study and these have answered satisfactorily.	
2.	I understand that my participation is voluntary and that if I take part, I am free to withdraw at any time, without giving a reason and without my medical care or legal rights being affected.	
3.	If in the course of the study I decide not to continue, I understand that any data collected up to the point of study withdrawal will be analysed.	
4.	I understand that if I lose the capacity to consent at any point during the study, additional tests or questionnaires will not be conducted for research purposes. In such a case, I agree for the researchers to use any previously collected research data and any further data collected as part of routine clinical practice.	
5.	I understand I will be given a Unique Identification Number (UIN) to ensure my data is pseudonymised.	
6.	I understand that researchers may contact me to follow up on my health status, remind me of upcoming study visits and remind me to respond to questionnaires for the AssistMS trial.	
7.	I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from the research team, study sponsor or delegate, regulatory authorities or the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	

8.	I understand that the information collected will be used for medical research only, including academic publications, and may be shared anonymously with other researchers.	
9.	I agree that my GP is being informed of my participation in the AssistMS trial.	
10.	I understand what is involved in the AssistMS study and agree to participate.	
11.	I agree that ico**metrix** retains a fully anonymised copy of my MRI data for future research / software development	

Optional		Please tick one		Initials
		Yes	No	
12.	I understand that I may be contacted by the research team in the future to be invited to take part in future studies. I understand that I would not have to take part in any upcoming research if I do not wish to.			
13.	I understand that information about me held by the treating hospital and relevant NHS organisation (NHS Digital in England) will be used to provide information about my health and treatments. To do this, my NHS number along with my sex, date of birth, and postcode will be shared with the relevant NHS organisation where I live. This will allow them to provide Queen Mary University of London with my de-identified personal data, which can only identify me by the study ID. I understand that any temporary computer files created for this purpose will be destroyed once the de-identified data has been transferred to Queen Mary University of London.			
14.	We may want to look at your health records (as described in Point 13 above) up to 10 years after you have joined to further see any changes in your health and treatments. I agree to my health records being used for future analysis.			

You will be provided with an electronic copy of this consent form.

Participants full name: _____

Signature: _____ Date: D D - M M M - Y Y Y Y

Witness's full name *(if applicable)*: _____

Signature: _____ Date: D D - M M M - Y Y Y Y

CONSENT OBTAINED BY

Investigator's full name: _____

Signature: _____ Date: D D - M M M - Y Y Y Y

eConsent will be managed by Castor EDC. PDF or hard copies can be generated. 1 copy for Participant, 1 for hospital medical notes and 1 to be kept in AssistMS Investigator Site File

[Site Logo]

[Site Address]