PODCAST STUDY
SUBSTANTIAL PROTOCOL AMENDMENT SUMMARY OF CHANGES VERSION, 1.2 to 1.4

Please note we have recently put forward a minor amendment (Version 1.3). The Nottingham Research Ethics Committee made the decision not to process the amendment as a minor amendment (email dated 28th April, 2011) so, to avoid confusion, we have moved to version 1.4 for the protocol. All forms requiring approval have been changed to version 1.4.

In the text below, protocol and information sheet changes, having implications for research design, conduct or participant safety have been listed. Additional, minor changes to text and formatting to bring protocol/information sheets and consent forms up-to-date are not described below but can be viewed in the 'marked' version of the protocol and information sheets.

PROTOCOL VERSION 1.4: SUMMARY OF CHANGES

The protocol has been version and date controlled.

1. All patients (ischaemic and haemorrhagic stroke) will now have fasting lipids, glucose and urea and electrolytes.

a. Addition in Section 3.5.1, 2nd paragraph, 1st sentence, Version 1.2 Protocol 22 July 2010
On the basis of the telephone assessments, if the participant is eligible and interested, a participant information sheet will be posted to the participant; a blood test request form (for lipid measurement) will also be sent for those participants whose index stroke was of ischaemic type.
Change to
On the basis of the telephone assessments, if the participant is eligible and interested, a participant information sheet will be posted to the participant; a blood test request form for fasting lipids, glucose and urea and electrolytes will also be sent.

b. Addition in Section 3.5.1, 3rd paragraph, 2nd sentence, Version 1.2 Protocol 22 July 2010.
If they have agreed, participants with ischaemic stroke will be asked to have the blood test (for lipids) done at their GP practice (with the posted blood test form).
Change to
If they have agreed, participants will be asked to have the blood test (for fasting lipids, glucose and urea and electrolytes) done at their GP practice (with the posted blood test form).

c. Addition in Section 3.5.4, 1st paragraph, 4th sentence, 3rd point, Version 1.2 Protocol 22 July 2010.
(iii) blood test for lipids

Change to
(iii) blood test for fasting lipids, glucose and urea and electrolytes

d. Addition in Section 3.5.4, 2nd paragraph, 1st sentence, Version 1.2 Protocol 22 July 2010.
If participants are eligible and interested, a participant information sheet along with a blood test form for lipids will be posted to them.

Change to
If participants are eligible and interested, a participant information sheet along with a blood test form for fasting lipids, glucose and urea and electrolytes will be posted to them

e. Addition in Section 3.6.1, 1st paragraph, 1st sentence, Version 1.2 Protocol 22 July 2010.
All participants will be followed up at six months and then annually at the local hospital research centre; a blood form for U&E and lipids (ischaemic stroke patients only) will be posted to the participants 2-3 weeks prior to each clinic visit

Change to
All participants will be followed up at six months and then annually at the local hospital research centre; a blood form for fasting lipids, glucose and urea and electrolytes will be posted to the participants 2-3 weeks prior to each clinic visit.

f. Page 18, **Table 3: has been updated to reflect the additional tests and measures**

2. Clarification that GPs will not be required to have GCP training.

Addition in Section 3.5.1, 2nd paragraph, last sentence, Version 1.2 Protocol 22 July 2010.
It is important to note that GPs will not be involved in screening and recruiting patients.
Change to
It is important to note that GPs will not be involved in screening and recruiting patients and therefore will not require Good Clinical Practice (GCP) certification.

3. 24 hour Ambulatory Blood Pressure Monitoring (ABPM) will be conducted at every clinic appointment for patients in the ABPM substudy.

Addition in Section 3.6.2.4, 1st paragraph, 1st sentence, Version 1.2 Protocol 22 July 2010.
In centres with the necessary ambulatory blood pressure monitoring equipment (e.g. SpaceLabs 90207), participants will have 24 hour ABPM [52] performed at recruitment and on treatment at 6 and 18 months.
Change to
In centres with the necessary ambulatory blood pressure monitoring equipment (e.g. SpaceLabs 90207), participants will have 24 hour ABPM [52] performed at recruitment and at all future scheduled clinic appointments.

4. The index event ECG will be collected at the Baseline visit. If facilities are available an ECG will be taken at each clinic visit and if the patient develops atrial fibrillation. **This will be added to Section 3.6.1, page 26, as the last sentence in the first paragraph.**

5. Addition in Section 3.5.7.3.2 Protocol Deviation, bullet point 2
Clinic or telephone assessments done outside the specified time by more than 30 days.
Change to
Clinic or telephone assessments done outside the specified time by more than 30 days. For the intensive BP group, clinic visits outside the specified time period by more than 14 days, or the time period between the visits is less than 2 weeks.

6. The exclusion criteria for liver function test have been revised.

Page 22 **3.5.3 Exclusion Criteria** 16. 'Liver disease, ALT>60 U/l' has been changed to 'ALT >3 times upper limit of normal, using local laboratories range'.

Page 21 Legend for figure 4 has been updated to reflect the above.

INFORMATION SHEET

The information sheet has been version and date controlled.

1. **Podcast Participant Information Sheet: Substudies V 1.2, 22 July**
2010 Page 2, last sentence:
The 24-hour monitoring will only be done on 3 occasions: at recruitment, 12
months and 24 months.
Change to
The 24-hour monitoring will be done at recruitment, and at all future scheduled clinic appointments.

2. **Participant Consent Form: Substudies v 1.1, 22 July 2010, Point 1.**
I confirm that I have read and understand the information sheet dated 22 July 2010 (Version 1.2) for the PODCAST sub studies and have had the opportunity to ask questions.
Change to
I confirm that I have read and understand the information sheet dated 26 April 2011 (Version 1.4) for the PODCAST sub studies and have had the opportunity to ask questions.

Point 4.
I agree to have 3 ambulatory blood pressure monitoring tests; on enrolment, and then at yearly intervals for another 2 years as explained in the information sheet.
Change to
I agree to have ambulatory blood pressure monitoring tests on enrolment, and then at each scheduled clinic appointment, as explained in the information sheet.

3**. Participant Information Sheet: Main study, Version 1.2, 22 July 2010**
The information sheet has been revised to reflect the changes made to the updated version of the protocol. The changes have been highlighted with track changes.

4. **Participant Consent Form: Screening, Version 1.2, 22 July 2010.**
Point 1 states: I confirm that I have read and understand the information sheet dated 22 July 2010 (Version 1.2) for the above study, and have had the opportunity to ask questions.
Change to
I confirm that I have read and understand the information sheet dated 26 April 2011 (Version 1.4) for the above study, and have had the opportunity to ask questions.

Point 3 states: I understand my general practitioner will be notified of my decision to agree for a telephone assessment of trial eligibility.

Point 3 now reads: I agree to be contacted at home for a telephone assessment of my memory, thinking and activities of daily living.

Point 4 states: I agree to be contacted at home for a telephone assessment of my memory, thinking and activities of daily living.

Point 4 now reads: I understand my general practitioner will be notified if I am eligible for the trial and wish to participate.

Point 5 states: I agree to have a blood test done to check my cholesterol levels (ischaemic strokes only).

Point 5 now reads: I agree to have a blood test done prior to my first clinic visit.

5. **Participant Consent Form: Main Study v1.2, 22 July 2010, point one of initial boxes**
I confirm that I have read and understand the information sheet dated 22 July 2010 version 1.2 for the above study, and have had the opportunity to ask questions.

Change to
I confirm that I have read and understand the information sheet dated 26 April 2011 version 1.4 for the above study, and have had the opportunity to ask questions.

6. **GP letter: diagnosis of probable dementia, version 1.1 dated 22 July 2010**
Paragraph 2 currently reads:
The low cognition score suggests that your patient may have developed dementia (Score <88 gives 94% sensitivity and 89% specificity, <82 gives 84% sensitivity and 100% specificity for dementia).

This has been changed to: Your patient's ACE-R score of <70 may suggest that your patient has developed dementia

7**. GP Letter: Practice Briefing Sheet, Version 1.0, 22 July 2010.**
The practice briefing sheet has been updated to include the addition of the glucose blood testing and the clarification regarding the GP not requiring GCP training. All changes are highlighted with track changes.

8. GP letter: enrolment, Version 1.2, 22 July 2010. *Blood tests*
All patients will be given a blood request form for U&E (Urea and electrolytes), and lipids prior to their local hospital research centre follow-up and will be asked to have the test done at their GP practice.

This should be:
Blood tests
All patients will be given a blood request form for urea and electrolytes, glucose and lipids prior to their local hospital research centre follow-up and will be asked to have the test done at their GP practice.