PODCAST: Prevention Of Decline in Cognition After Stroke Trial

GP LETTER: PRACTICE BRIEFING SHEET

(adopted from the EMSY PCRN template[1])

Sponsor: The University of Nottingham
Chief Investigator: Professor Philip Bath

Local Investigators:.....

The practice briefing is an outline of the research protocol and information source for the general practices that collaborate with the researchers.

Title of Project:

Prevention Of Decline in Cognition After Stroke Trial (PODCAST): A factorial randomised controlled trial of intensive versus guideline lowering of blood pressure and lipids.

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Principal Investigator at this site:

[1] East Midlands and South Yorkshire Primary Care Research Network

Proposed starting and finishing dates:

Start Date: 1 September 2010

End Date: 31 August 2018

Funding bodies and amounts:

Research Costs - £399,145 - 50:50 co-funding by The Stroke Association UK and Alzheimer's Society UK.

Service support costs (SSC) - funded by NHS through Comprehensive Local Research Networks (CLRN).

Excess treatment costs (ETC) - funded by NHS through Primary Care Trusts (PCT).

Idea behind the project and outline of study design:

Background

Approximately 30% of people who have a stroke, go on to develop cognitive problems, and then dementia. Both stroke and dementia are devastating, causing people to lose their independence, so that they need care from family or in an institution. Both conditions are very expensive to society through lost work, healthcare and family-care costs, and being in an institution.

There are no licensed treatments for these people and little investment in research. Although several blood pressure lowering studies have assessed cognition, the results are not conclusive, as cognition was only ever a secondary outcome. Nevertheless, it appears that lowering blood pressure may delay or reduce cognitive decline. Lowering cholesterol could reduce cognitive decline, in part by preventing stroke, but the evidence to date is limited.

A large, well designed study is urgently needed to test whether intensive treatment of high blood pressure and high cholesterol can reduce the number of people developing a decline in cognition, and dementia after stroke. If the trial is positive, the interventions are readily available and can be introduced into the NHS rapidly and inexpensively so that the risk of cognitive impairment and dementia can be reduced by 20% or more in stroke survivors.

Project Aims

Primary: To determine if 'intensive' blood pressure lowering therapy, and/or 'intensive' lipid lowering therapy, reduces cognitive decline and dementia after stroke.

Secondary: To determine if 'intensive' blood pressure lowering therapy, and/or 'intensive' lipid lowering therapy, reduces poor quality of life, poor function, depression, stroke recurrence, vascular events, and death, after stroke.

Overview of the trial

The trial will run in two phases. The start-up feasibility phase will aim to recruit 600 patients across the UK in the first 3 years, and the main phase, a further 2,800 participants from across 100 sites internationally over the next 5 years (total 8 years).

Participants with confirmed ischaemic or haemorrhagic stroke, 3-7 months post event, who satisfy the inclusion and exclusion criteria will be randomised to the 'intensive' or 'guideline' BP management group by the hospital researchers. Participants with an ischaemic stroke (but not haemorrhagic) will also be randomised to the 'intensive' versus 'guideline' lipid-lowering arm.

The 'intensive' BP lowering group will aim for a SBP <125 mmHg, and the 'guideline' group a SBP<140 mmHg. The 'intensive' lipid-lowering group will aim for a target LDL cholesterol <1.4 mmol/l, and the 'guideline' group a target LDL-cholesterol of <3.0 mmol/l. The number of drugs and/or doses in the 'intensive' group will be escalated on review at the hospital research centre; the guideline groups will be managed by their GP, as per current guideline recommendations.

Cognition and other outcome data will be collected at baseline and six monthly follow-ups (alternating research clinic and telephone follow-up) for up to 8 years. An interim analysis will be performed at the end of the start-up phase (3 years) to assess feasibility.

Study participants will be recruited from the local hospital, consented in the hospital's research clinic, and be randomised to:

- Intensive or guideline BP lowering (all participants)
- Intensive or guideline lipid lowering (ischaemic stroke only)

As a result, patients can be randomised to one of 6 groups:

- *Intensive BP lowering and intensive lipid lowering (ischaemic stroke only)*
- *Intensive BP lowering and guideline lipid lowering (ischaemic stroke only)*
- *Guideline BP lowering and intensive lipid lowering (ischaemic stroke only)*
- *Guideline BP lowering and guideline lipid lowering (ischaemic stroke only)*
- *Intensive BP lowering (intracerebral haemorrhage only)*
- *Guideline BP lowering (intracerebral haemorrhage only*)

Outline of consumer involvement in the research project:

The trial is supported by the:

- Alzheimer's Society Quality Research in Dementia Consumer Advisory Network
- Stroke Research Network Prevention Clinical Studies Group
- Trent Stroke Consumer Group.

Three members of the Patient, Carer and Public Involvement Group have specifically reviewed and advised on the content of the information sheets.

What is expected of the GP practices?

Recruitment and consent will not involve GPs. All trial case report forms will be completed at the recruiting hospital (for clinic data) or by the Coordinating Centre (for telephone data). **No data forms will need to be completed by GPs.**

Blood Tests

GP practices will be asked to perform blood tests for fasting lipids, U&E (urea and electrolytes), glucose and HbA1c, prior to baseline and 6 monthly clinic visits. **The request for these tests will come from the local hospital research centre and GP practices are not expected to chase patients for these blood tests.**

Additional monitoring blood tests will be performed for patients in the intensive groups:

- For patients in the intensive BP group, additional blood tests for U&Es will be performed 1-2 weeks prior to the hospital visit at 1, 2 and 3, months.
- For patients in the intensive lipid group, blood tests for fasting lipids (TC, TG, HDL) will be performed 1-2 weeks prior to the hospital visit at 3 months.

Management and Prescriptions

For intensive BP and lipids groups, prescriptions should be continued as suggested by the local hospital research team, unless there is a significant clinical reason to change therapy. Please let the hospital research team know if therapy is changed.

For guideline BP and lipids groups, GPs will treat trial participants as is their usual practice, based on current guidelines**.**

Good Clinical Practice (GCP) Certification

As GPs are not involved in screening or randomising patients, they are not expected to be GCP trained to be part of the study.

The implications for the practice's patients

Intensive treatment of BP and lipids after stroke may prevent cognitive decline and recurrent stroke after stroke although no promises will be made.

What the practice will be offered (feedback, finance etc.)

Relevant information on participants regarding BP, lipids, other vascular prophylaxis, life style advice etc. will be fed back to the GPs. Such information may be useful for patient records and returns for Quality and Outcomes Framework indicators.

The funding for performing blood tests will come from the service support costs through the PCRN and each participating practice will be reimbursed for the blood tests they perform. The exact amount to be reimbursed to each GP practice will depend on the group the patient is randomised to.

The excess treatment costs for participants in the PODCAST study has been approved by your Primary Care Trust.

Other information

GPs should continue to conduct other necessary checks / blood tests for study participants, as per their usual practice and based on current guidelines. For example, this might include performing lying/standing BP measurements in patients with falls, blood creatine kinase (CK) for patients complaining of muscle pain and tenderness (as a potential adverse event associated with statins).

If your practice uses the Script Switch or other such software that provides treatment suggestion based on costs, please remember to ignore its advice when prescribing for patients in the trial.