PB-PG-1208-17114 – NIHR Research for Patient Benefit Programme – Final report

Project title: IMPROVE-Stroke: IMproving the PRevention Of Vascular Events after Stroke or TIA – a randomised controlled pilot trial of nurse independent prescriber-led care pathway-based risk factor management

Authors:Dr Martin James - Royal Devon & Exeter NHS Foundation Trust
Professor Nicky Britten - University of Exeter Medical School
Dr Colin Pritchard -
Professor Sue Latter - University of Southampton
Dr Phillip Evans - University of Exeter Medical School

Plain language summary:
In the IMPROVE pilot study we set out to test the feasibility and practicality of an intervention designed to improve the uptake of preventative treatments after a stroke or a TIA. The intervention was based around the input of a new type of nurse, called a 'Nurse Independent Prescriber', who monitors and treats a person's risk factors (mainly their cholesterol and blood pressure) using a treatment plan called a care pathway. The intervention lasted 6 months from when a person suffered their stroke or TIA, and we compared it with receiving treatment the usual way, from the person's GP at the local surgery. As this was a pilot study, we were not expecting to be able to prove definitely that the intervention was better than 'usual care', but only seeking to prove that it was feasible and acceptable to follow people up in this way, and to iron out any problems in advance of a much larger study designed to give a definite answer.

We found that it was possible to recruit nearly as many people as we expected into the study over the 8 month recruitment period - we recruited 32 people when we wanted to recruit 40. We found that being in the study was perfectly acceptable to participants, and far from feeling burdened by the frequency of follow-up visits, people reported being reassured that someone was taking such a close interest in their risk factors, and that they were seeing the same nurse each time. As a result, no-one dropped out of the study during the 6 month intervention period. We also found that the intervention was acceptable to GPs, who were happy to receive the additional support that the nurse offered.

We found that the use of the care pathway did not cause more adverse effects (side-effects) than we would have expected for anyone being treated for blood pressure. Using the care pathway did result in a substantial fall in people's blood pressure measured in the clinic, to a greated extent than we saw in people receiving 'usual care', although that difference was less when we measured people's blood pressure at home using an automatic device.
Taken overall, we were very encouraged by the results of the pilot study and did not encounter any major problems. This has encouraged us to propose a larger study that should give us a definite answer as to whether this 'care pathway' method is better than existing care, involving over 600 patients in a collaboration between Devon and Leicester, and this has been submitted for grant funding.

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Ischemic Attack, Transient [C10.228.140.300.150.836]

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Blood Pressure[E01.370.600.875.249]

Summary of research findings:

Background
There is good evidence of a gap between the findings from randomised controlled trials (RCTs) that risk factor modification after stroke or transient ischaemic attack (TIA) prevents further vascular events, and the implementation of those findings in clinical practice. The resulting failure to fully implement the existing evidence jeopardises the large benefits to patients and the NHS that should otherwise accrue, yet evidence to support effective risk factor management strategies in Primary Care after stroke is lacking. One novel approach may be care led by a Nurse Independent Prescriber, and a recent Cochrane review concluded that this form of intervention warrants further evaluation. However, such a novel and complex intervention requires pilot data prior to a definitive RCT.

Aims and objectives
The IMPROVE pilot study was planned as a prelude to a definitive RCT assessing the effectiveness and cost-effectiveness of a Nurse Independent Prescriber-led care pathway for risk factor management after stroke or TIA compared to 'usual care'. The aim of the pilot was to ensure the design and methods of the definitive RCT were sound, practicable and feasible.
The objectives of the pilot were:
1. To test the feasibility, practicality, safety and acceptability of the study design and protocol;
2. To resolve practical issues for the conduct of the future RCT such as the reproducibility of the outcome measures, and recruitment and attrition rates;
3. To investigate the acceptability of the care pathway to patients and general practitioners (GPs) and to refine it prior to the full RCT;
4. To inform the sample size calculation for the full trial.

Methods
Study Design
A prospective, cluster-randomised controlled open pilot trial with a nested qualitative study. Two clusters of general practices (Exeter city and the west half of East Devon) were randomised, with the Exeter cluster allocated to the intervention and the East Devon cluster as control. Patients registered with a GP within these clusters who met the inclusion criteria and who gave informed consent without prior knowledge of the randomisation status of their cluster were allocated to the relevant group.

Study Recruitment
The recruitment target was 40 patients within one month of a new diagnosis of stroke or TIA. Study duration for each participant was 12 months.

Inclusion Criteria
• Clinical diagnosis of TIA or stroke within one month
• Patient living at home at time of recruitment
• Age >18 years
• SBP >140 mmHg measured at time of diagnosis of stroke or TIA

• Registered with a GP in one of the two pilot clusters
• Ability to attend for follow-up visits
• Informed consent

Exclusion Criteria
• Severe dementia or aphasia
• Significant co-morbidity likely to jeopardise ability to complete the trial e.g. malignancy, severe heart failure
• Current participation in other trials.

Recruitment and baseline visit
Eligible patients were recruited from the daily Rapid Access Stroke Clinic or the Acute Stroke Unit at the Royal Devon and Exeter Hospital. All study visits took place in clinics in two local community hospitals. After consent, demographic data, medical history, medication knowledge, smoking history and total and LDL cholesterol were collected. Disability was measured using the Modified Rankin Scale (mRS) and health related quality of life (QoL) with the EuroQOL EQ-5D. The participant's clinic BP was measured as the mean of three readings after 5 minutes seated using an Omron M6 semi-automatic monitor. An ambulatory BP monitor (SpaceLabs 90207) was fitted, set to measure BP every 30 minutes for 12 hours during normal activities; stored BP data was downloaded to a PC from the monitor.

Statistical Analysis
As a pilot study, no formal sample size calculation was made. The primary outcome was the difference in systolic BP between intervention and usual care at 6 months. Formal statistical comparisons were not planned and so study outcomes are presented in purely exploratory terms.

Key findings/results
32 patients (mean age 72 years SD 9, range 46-89; 12 female) within one month of TIA or stroke were recruited over 8 months, against a recruitment target of 40 (80% of target). 40% of eligible patients were recruited. 18 participants came from practices randomised to the intervention (the Exeter cluster), and 14 from practices randomised to usual care (the East Devon cluster). Only 2 patients were current smokers.
Clinic and ambulatory BP were different at baseline between the two groups: intervention clinic BP 151/86, ambulatory BP 130/80; control clinic BP 159/84, ambulatory BP 139/78. Baseline mean total and LDL cholesterol (in mmol/L) were similar: intervention total 4.6, LDL 2.5; control total 4.2, LDL 1.7.

6-month outcomes
All patients completed the 6 month assessment (100% retention for the primary outcome measure). Nurse prescriber-led care resulted in a greater number of antihypertensive drug classes being prescribed (intervention 2.6, control 1.7; mean diff = 0.85; 95% CI: 0.2-1.5, P=0.01) and more net dosage increments being made (intervention 2.8, control 0.9, mean diff = 2.0; 95% CI: 1.1- 2.9, P<0.001) over the 6 months of the intervention. Clinic BP (in mmHg) was significantly lower in the intervention group at 6 months (intervention v. control SBP 130 v. 149; DBP 75 v. 82; P=0.02) but the between-group difference in ambulatory BP was less, and not statistically significant (SBP 124 v. 132; DBP 72 v. 73). This represented a mean reduction of 20 mmHg in clinic BP and of 6.7 mmHg in ambulatory BP for the

intervention group, and reductions of 10 mmHg in clinic BP and 7.4 mmHg in ambulatory BP for the control group. The proportion of participants who reached their target BP at 6 months was 66% in the intervention group and 7% in the control group. Total and LDL cholesterol were not different between the two groups at 6 months at 4.3 mmol/L and 2.1 mmol/L respectively in both groups.
There were three recurrent vascular events during the 6 month study period (2 TIAs and one stroke) and no deaths. The number of healthcare practitioner contacts was lower in the intervention group at 8.7 v. 13.1; the number specifically in relation to secondary vascular prevention was also lower at 4.2 v. 9.1. The mean number of contacts with the Nurse Independent Prescriber in the intervention group was 6.8.
Medication knowledge, self-reported medication adherence, health-related quality of life and disability did not differ between intervention and control groups at baseline, 6 months or 12 months.

12 month outcomes
30 patients were followed up after 12 months, with 2 dropouts between 6 and 12 months (one due to ill health, one participant left the area). Broadly, BP changed little between 6 and 12 months, during which period all participants continued with or were returned to usual care. At 12 months clinic BP remained significantly lower in the intervention group (SBP 131 v. 147; DBP 75 v. 82 mmHg; P=0.02) but ambulatory BP rose slightly in both groups, although the difference in ambulatory BP between the groups remained smaller than with clinic BP (SBP 126 v. 135; DBP 73 v. 76 mmHg). Total and LDL cholesterol remained no different between the two groups at 4.3 mmol/L and 2.1 mmol/L respectively.

Qualitative sub-study
Thirty-one patients and 16 significant others were interviewed. The significant others were mainly the patient's partner/spouse (n=14). Overall, the study methods and the intervention proved highly acceptable to patients. Patients and their significant others appreciated receiving monitoring and reassurance, and did not find the intervention burdensome despite the frequency of follow-up and medication adjustment (as much as fortnightly). The relationship patients had with their health professional, and the role the health professional played, were key in meeting the need for monitoring and reassurance. The nurse prescriber intervention met the patients' needs for monitoring and reassurance and patients welcomed their specialist role and expertise. Adherence to medication was similar (high) across both groups, however there were other, 'softer' outcomes related to perceived quality of care, relationship with health professionals, and 'peace of mind' that also featured prominently in the patient experience. There were perceived barriers to accessing the GP and to receiving regular and pro-active feedback and review, both features of the new intervention that were highly rated by participants.

Expected Impact
The principal impact of the IMPROVE pilot study has been in demonstrating the feasibility and practicality of the new nurse prescriber-delivered intervention and in reinforcing the rationale for the methods proposed for the definitive RCT. The intervention proved universally acceptable to both participants and their GPs, and required the minimum of modification during the pilot period to eliminate minor inconsistencies, mainly in relation to the point in the pathway a patient would join if they already had existing antihypertensive

treatment. Adverse effects were minimal, as might be expected from an incremental algorithm using well established therapeutic agents.

Conclusions
The IMPROVE pilot study achieved its aim, and has provided valuable pilot data on which to base the design of the definitive RCT. The exploratory quantitative data do suggest an impact of the intervention in terms of a greater degree of antihypertensive up-titration and prescribing, and the suggestion of a potential impact at least on clinic BP - an effect not mirrored in the much simpler area of cholesterol-lowering treatment. The intervention was not burdensome to participants, instead being well received by patients and their GPs. No major modifications to the protocol have been required before scaling up the design to the level of statistical power required to definitively test the effectiveness and cost-effectiveness of the intervention in a large RCT.

Patient and public involvement
The South West Stroke Research Network (SWSRN) held three workshops in the peninsula during 2008 involving over 70 patient and carers, including people with aphasia, to explore the patient experience after stroke and address the issue ‘What questions still need answering by research?’. Among a wide range of issues raised were ‘Investigating better ways of treating those at risk of secondary strokes’, ‘Investigating the potential for ongoing BP monitoring by a specialist nurse after stroke’, and ‘Should there be long-term follow-up by hospital consultants after stroke, particularly for medication?’. Our study, submitted for funding in 2009, emerged in part from these issues raised by people with stroke.

Early drafts of the proposal and Lay Summary were circulated to a group of 23 patients and carers prepared to act as reviewers for research proposals in the SWSRN. It received enthusiastic support from people with stroke, who emphasized the importance of simple and widely applicable measures to prevent stroke, the importance of proving that treatments were effective over the long term and not just the short term, and the potential benefits of regular and systematic follow-up. The study design took account of this feedback.

During the study design, the co-applicants held one two-hour focus group with 11 people with stroke and their carers, addressing both the quantitative and qualitative elements of the design. There were some significant modifications resulting from that activity, such as an increased emphasis on the non-pharmacological management of risk factors, the inclusion of carers in the qualitative interviews, and a longer period of follow-up.

We appointed four stroke survivors to the Trial Management Group (TMG), and although one withdrew after a year due to poor health, the remaining three were regular attenders and active participants in the management of the trial without tokenism, providing valuable advice and insights on issues relevant to patient participation. One TMG member is also on the editorial group for the SWSRN PPI Newsletter, which is distributed quarterly to a mailing list of over 400 people with stroke/TIA and also distributed via stroke research staff in the SWSRN's 17 research-active centres. This member authored two articles regarding IMPROVE-Stroke for the newsletter, one at the outset and the other at the conclusion of the study. Based on our PPI experience with the IMPROVE pilot study, we plan an even greater

degree of PPI and public dissemination for the definitive RCT presently with the HTA-CET programme.

Data sharing statement

See link [https://www.nihr.ac.uk/documents/nihr-position-on-the-sharing-of-research-data/12253] for the NIHR position of the sharing of research data. The NIHR strongly supports the sharing of data in the most appropriate way, to help deliver research that maximises benefits to patients and the wider public, the health and care system and which contributes to economic growth in the UK. All requests for data should be directed to the award holder and managed by the award holder.

Disclaimer

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This project was carried out between December 2010 and November 2012. This final report has not been peer-reviewed. The report was examined by the Programme Director at the time of submission to assess completeness against the stated aims.