The Stroke Prevention Programme: a programme of research to inform optimal stroke prevention in primary care

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Scientific summary

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Background

Management of cardiovascular (CV) risk factors in community populations remains suboptimal, despite impact from interventions such as the Quality and Outcomes Framework. The aim of this programme was to explore the role of three approaches [use of a 'polypill'; self-management of hypertension; and more intensive targets for blood pressure (BP) lowering after stroke] to improve prevention of CV disease (CVD) in the community.

Objectives

The programme aimed to answer the following research questions.

On the potential role of a polypill:

- What is the prevalence of 'high CV risk' and use of CV-risk-lowering treatments in people aged ≥ 50 years in primary care?
- What is the impact of age and sex on primary preventative treatment for CVD?
- What is the prevalence of 'high CV risk' among people with unknown risk aged ≥ 50 years in primary care?
- What are patient and practitioner views of using a polypill to manage their CV risk as opposed to treatment by monitoring targets?
- What is the cost-effectiveness of primary prevention of CVD with a polypill for all versus screen and treatment as per guidelines in a population with unknown CV risk?
- What is the cost-effectiveness of the use of a polypill versus usual care or best practice for primary prevention in high-risk patients?
- What is the prevalence of stage 1 hypertension?
- From a patient perspective, how feasible is a primary prevention trial of a polypill in people of unknown CV risk?

On self-management of BP:

- Does self-monitoring reduce BP?
- Does self-management reduce BP in hypertensive people with poorly controlled BP?
- What are patients' experiences of self-management of BP?
- What are health-care professionals' experiences of looking after patients who are self-managing their BP?
- Is self-management of BP cost-effective for people with uncontrolled hypertension?
- Does self-management reduce BP in people with stroke and other high-risk groups?
- What were patients' experiences in participating in a trial of self-management?
- Is self-management of BP cost-effective for people with stroke and other high-risk groups?

On BP targets for people with stroke:

- Can intensive BP targets be achieved in a community population of people with prevalent cerebrovascular disease?
- What are the views of people with stroke on the role of BP and how it should be managed?
- Is aiming for intensive BP targets cost-effective in people with prevalent cerebrovascular disease?

Methods and results

Potential role of a polypill

We carried out a cross-sectional retrospective study of electronic primary care medical records of all patients aged > 40 years (for some analyses the age range was restricted to 40–74 years) registered with 19 general practices in the West Midlands. Of 34,975 patients (aged 40–74 years) included in this study, 2550 (7%) had existing CVD and 12,349 (35%) had a calculable CVD risk or were on treatment. CVD risk was formally assessed in 8390 (24%) patients. Approximately 7929 (64%) patients eligible for primary prevention therapy were being treated appropriately for their CVD risk. The proportion receiving antihypertensive drugs rose with age from 5% (378/6978) aged 40–44 years to 57% (621/1092) aged ≥ 85 years, as did the percentage taking a statin up to the age of 74 years [from 3% (201/6978) aged 40–44 years to 29% (675/2367) aged 70–74 years]. In those aged ≥ 75 years, the odds of receiving a prescription for a statin (relative to the 40–44 years age group) decreased with every 5-year increment in age [odds ratio 12.9, 95% confidence interval (CI) 10.8 to 15.3 at the age of 75–79 years to 5.7, 95% CI 4.6 to 7.2 at the age of ≥ 85 years; $p < 0.001$]. There were no consistent differences in prescribing trends by sex. Of the 34,975 patients in this study, untreated and uncomplicated stage 1 hypertension was present in 2867 individuals (8.2%). The additional cost of controlling BP according to international guidelines for England and Wales was estimated to be between £106M and £229M per annum depending on the health-care professional delivering care.

A screening study was carried out in which patients aged ≥ 50 years who were of unknown CV risk were invited to attend their practice for a screening assessment. Of screened patients, 69% were found to have a 10-year risk of CVD of < 20%, 29% were found to have a 10-year risk of CVD of > 20%, 1% were found to have existing CVD and for 1% the risk could not be calculated. For a population aged ≥ 50 years, estimates are that 53% have 'low' risk of CVD, 30% have 'high risk' of CVD and 17% have existing CVD.

Semistructured interviews were undertaken with 16 primary health-care professionals and 17 patients who had existing CVD or were identified as being at high CV risk. For health-care professionals, there was considerable resistance towards the use of a polypill for the prevention of CVD in people not regarded as being at 'high risk'. Evidence of efficacy was judged important but potential medicalisation and an ongoing need for monitoring were significant issues for many health-care professionals. Patients also had reservations with regard to using a polypill for primary prevention, except in people already known to be at high risk, although concerns were expressed around inflexibility of dosing.

A cost-effectiveness analysis using a Markov model with a monthly time cycle and a lifetime horizon was used to estimate the cost per quality-adjusted life-year (QALY) of two prevention strategies for patients aged ≥ 50 years with unknown CV risk and no history of CVD who were not on statins or antihypertensive therapy. Individual patient-level data were used from a screening study. Published sources were used to estimate the impact of the different treatment strategies on the risk of CV events and their associated costs and utilities. The polypill was assumed to contain simvastatin (40 mg), hydrochlorothiazide (12.5 mg), lisinopril (5 mg) and amlodipine (2.5 mg). Best practice was based on the National Institute for Health and Care Excellence guidelines for lipids and hypertension published in 2010 and 2011, respectively. For people with unknown CV risk aged ≥ 50 years, offering a polypill is cost-effective (incremental cost-effectiveness ratio of £8115 per QALY) compared with a strategy of screening and treating according to national guidelines. The result is sensitive to the cost of the polypill.

A cost-effectiveness analysis using a Markov model with a 1-year time cycle and a 10-year horizon was used to estimate the cost per QALY of three CV prevention strategies for people aged ≥ 40 years. Individual patient-level data were used from the retrospective cross-sectional study of primary care medical records. For patients known to be at high risk of CVD, treatment as per guidelines was the most cost-effective strategy. However, if the cost of the polypill was ≤ £150 per annum, the polypill became the most cost-effective option.

A postal survey was conducted of patients of unknown CV risk from a single general practitioner (GP) practice. In that single practice, 25 people of unknown CV risk were identified who said that they would give consent to take part in a polypill versus screening trial.

Self-management of blood pressure

In the systematic review, relevant databases were searched for studies in which the intervention included self-monitoring of BP and the outcome was change in BP. Two reviewers independently extracted data. Meta-analysis using a random-effects model was combined with meta-regression to investigate heterogeneity in effect sizes. A total of 25 eligible randomised controlled trials (RCTs) were identified. Systolic BP was significantly reduced in those who self-monitored compared with usual care (weighted mean difference systolic 3.8 mmHg, 95% CI 5.6 to 2.0 mmHg).

There was significant heterogeneity between studies for all three comparisons, which could be partially accounted for by the use of additional cointerventions.

The RCT TASMINH2 (Telemonitoring and Self-Management in the Control of Hypertension) recruited patients aged 35–85 years from general practices in the West Midlands who had BP of ≥ 140/90 mmHg despite antihypertensive treatment and were willing to self-manage their hypertension. Intervention comprised self-management, consisting of self-monitoring of BP and self-titration of antihypertensive drugs, combined with telemonitoring of home BP measurements. The comparison arm was usual care. Neither participants nor investigators were masked to group assignment. The primary end point was change in mean systolic BP between baseline and each follow-up point (6 months and 12 months). All randomised patients who attended follow-up visits at 6 months and 12 months and who had complete data for the primary outcome were included in the analysis, without imputation for missing data. Systolic BP decreased by 17.6 mmHg (95% CI 14.9 to 20.3 mmHg) over 1 year in the self-management group and by 12.2 mmHg (95% CI 9.5 to 14.9 mmHg) in the control group (difference between groups 5.4 mmHg, 95% CI 2.4 to 8.5 mmHg; $p = 0{\cdot}0004$).

Qualitative studies were embedded within the RCTs. Semistructured interviews were conducted with 23 intervention patients, six family members and 16 health-care professionals (13 GPs, two practice nurses and one health-care assistant). Analysis used a constant comparative method. Patients were confident about self-monitoring and considered that it improved accuracy. Some lacked confidence to self-manage medication without reconsulting with their GP, especially if their BP readings were only just above target. Many planned to continue self-monitoring after the study finished and report home readings to their GP, but few wished to continue with a self-management plan. Primary care professionals were positive about self-monitoring, but procedures for ensuring patients measured BP correctly were haphazard. GPs interpreted home readings variably, with many not making adjustment for lower home BP. There was evidence of a need for training of both patients and professionals for the successful integration of self-management.

Cost-effectiveness analysis of the TASMINH2 intervention used a Markov model using cost and outcome data collected from a RCT and extrapolating to a 35-year time horizon using the literature on the association between BP and CV outcome. Self-management was cost-effective at £1624 per QALY for men and £4923 per QALY for women. There was at least a 99% chance of the intervention being cost-effective for both sexes at a willingness-to-pay threshold of £20,000 per QALY gained. These results were robust to sensitivity analyses around the assumptions made, provided that the effects of self-management lasted at least 2 years for men and 5 years for women.

A RCT (Targets and Self-Management for the Control of Blood Pressure in Stroke and at Risk groups; TASMIN-SR) was conducted of self-management of BP versus usual care. Eligible patients had a history of stroke, coronary heart disease, diabetes or chronic kidney disease and were individually randomised to usual care or self-management. Patients were recruited from practices in the West Midlands and the east of England. Self-management comprised self-monitoring of BP combined with an individualised

self-titration algorithm agreed at baseline. A target of < 130/80 mmHg adjusted for home measurement was used in all groups. The primary outcome was the difference in office systolic BP between intervention and control at 12 months. Baseline BP was 143.0/80.4 mmHg (intervention) and 143.2/79.7 mmHg (control). After 12 months this had dropped to 128.0/73.7 mmHg (intervention) and 137.4/76.4 mmHg (control), a difference of 9.2 mmHg (95% CI 5.7 to 12.7 mmHg) in systolic and 3.4 mmHg (95% CI 1.8 to 5.0 mmHg) in diastolic following correction for baseline BP and covariates. These results were robust to sensitivity analyses, were similar in all subgroups examined and did not result in an excess of side effects.

Participants in the TASMIN-SR trial were given a blank postcard at their 12-month follow-up and invited to write about their trial experiences. Respondents ($n = 148$) reported benefits from trial participation, including personal satisfaction, greater involvement in their own care and better understanding about hypertension and the importance of lifestyle.

Cost-effectiveness analysis of the TASMIN-SR intervention used a Markov model with a 1-year time cycle and a 30-year time horizon using cost and outcome data collected from a RCT and literature on the association of BP with CV outcome. Self-management of hypertension in people with stroke or other high-risk conditions is cost-effective and a dominant strategy.

Intensive blood pressure lowering in people with prevalent cerebrovascular disease

A RCT was conducted of patients with a history of stroke or transient ischaemic attack (TIA) whose BP was ≥ 125 mmHg and who were not already on three or more antihypertensive drugs were recruited. Participants were randomly assigned to an intensive systolic BP target (< 130 mmHg or 10 mmHg reduction from baseline if this was < 140 mmHg) or a standard target (< 140 mmHg). Participants were recruited from practices in central, east and north-east England. Apart from the different target, patients in both arms were managed in the same way with regular reviews by the primary care team. The primary end point was change in systolic BP between baseline and 12 months. A total of 529 patients, mean age 72 years, were enrolled, 266 to the intensive target arm and 263 to the standard target arm, of whom 379 were included in the primary analysis (182, 68% intensive arm; 197, 75% standard arm). 84 patients withdrew from the study during the follow-up period (52 intensive arm and 32 standard arm). Mean systolic BP dropped by 16.1 mmHg to 127.4 mmHg in the intensive target arm and by 12.8 mmHg to 129.4 mmHg in the standard arm (difference between groups 2.9 mmHg, 95% CI 0.2 to 5.7 mmHg; $p = 0.03$).

Semistructured interviews were conducted with health-care professionals and patients participating in the RCT, together with a small sample ($n = 4$) of patients who had declined trial participation. Health-care professionals had concerns over the feasibility of the intensive targets because of side effects, and questioned the value of the trial. Patients in general accepted the advice of their doctors.

Cost-effectiveness analysis of the PAST-BP (Prevention After Stroke – Blood Pressure) intervention used a Markov model with a 1-year time cycle and a 30-year time horizon using cost and outcome data collected from a RCT and literature on the association of BP with CV outcome. Self-management of hypertension in people with stroke or other high-risk conditions is cost-effective and a dominant strategy.

In the base-case scenario, aiming for an intensive BP target was dominant, with the incremental lifetime costs being £130 per patient lower than for the standard BP target, with a 0.08 QALY gain. If the time horizon was shortened, the cost-effectiveness of an intensive target fell.

Conclusions

The potential for a polypill needs to be further explored in RCTs. Self-management should be offered to people with poorly controlled BP. The management of BP in the post-stroke population should focus on achieving a < 140 mmHg target.

Research recommendations

- A RCT of offering a polypill against offering health checks in people aged ≥ 50 years.
- Qualitative research should be carried out to better understand the attitudes of older people (aged ≥ 80 years) to taking drugs to reduce risk of CVD.
- A RCT of statin therapy for prevention of CVD in people aged ≥ 80 years.
- A RCT of management of hypertension based on self-monitored BP readings.
- A RCT of self-management of hypertension that is sufficiently powered to detect impact on clinical end points.
- Development and evaluation of interventions to improve active management of BP in people after a stroke/TIA to achieve a target of < 140 mmHg systolic BP.

Trial registration

These trials are registered as ISRCTN17585681, ISRCTN87171227 and ISRCTN29062286.

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