# Different systolic blood pressure targets for people with a history of stroke or transient ischaemic attack, the PAST-BP (Prevention After Stroke – Blood Pressure) study: randomised controlled trial

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**Abstract**

*Objectives:*  Blood pressure lowering is effective at reducing risk of stroke recurrence in people who have had a cerebrovascular event, but it is uncertain how low blood pressure should be lowered in this population. We assessed whether using intensive blood pressure targets would lead to lower blood pressure in a community population of people with prevalent cerebrovascular disease.

*Design:*  Open label randomised controlled trial.

*Setting:*  99 General Practices in England, with participants recruited 2009-2011.

*Participants:* People with a history of stroke or transient ischaemic attack whose systolic blood pressure was ≥ 125 mmHg.

*Interventions:* Intensive systolic blood pressure target (<130mmHg or 10mmHg reduction from baseline if this was < 140 mmHg) or a standard target (<140mmHg).  Apart from the different target, patients in both arms were actively managed in the same way with regular reviews by the primary care team.

*Main outcome measure*:  Change in systolic blood pressure between baseline and twelve months.

*Results*: 529 patients, mean age 72, 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; 32 standard arm).  Mean systolic blood pressure dropped by 16.1mmHg to 127.4mmHg in the intensive target arm and by 12.8mmHg to 129.4mmmHg in the standard arm (difference between groups 2.9 mmHg, 95% confidence interval (0.2 to 5.7); p = 0.03).

*Conclusions:*  Aiming for target below 130mmHg for systolic blood pressure in people with cerebrovascular disease in primary care rather than <140mmHg leads to a small additional reduction in blood pressure.  Active management of systolic blood pressure in this population using a <140mmHg target leads to a clinically important reduction in blood pressure.

*Trial Registration*:  ISRCTN29062286.

**Introduction**

Stroke accounts for about 10% of deaths internationally, and for over 4% of direct health care costs in developed countries. [1] If other resources, such as lost productivity, benefits payments and informal care costs are taken into account, the total costs double – for example in the United Kingdom annual care costs are around £4.4 billion, but total costs are £9 billion per annum. [2] Over 20% of strokes are recurrent events, [3] and if one also takes into account prior history of transient ischaemic attack (TIA), this figure rises to about 30%. [1] Therefore, secondary prevention has a major potential role to play in reducing both morbidity and costs of stroke care. Hypertension is a key risk factor for stroke. A 20 mm Hg difference in usual systolic blood pressure is associated with a 60% lower risk of death from stroke in someone aged 50 to 70, and a 50% lower risk in someone aged 70 to 79. [4]

The PROGRESS trial demonstrated that treatment to lower blood pressure in people who have had a stroke or TIA reduces risk of further stroke. [5] However, there is debate over how to apply this evidence in clinical practice. [6][7] In particular, there is uncertainty over how intensively to lower blood pressure in people who have had a stroke or TIA. [8] A post hoc observational analysis of the PROFESS trial found that people with recent ischaemic stroke whose systolic blood pressure was less than 130mmHg had a higher risk of vascular events. [9] Conversely, in PROGRESS participants whose baseline systolic blood pressure was 120-140mmHg who were randomised to combination therapy had significantly reduced stroke risk. [10] The SPS3 trial of different blood pressure targets in younger (mean age 63) patients with recent lacunar stroke found a non-significant 19% reduction in risk of stroke after one year in people treated with a systolic blood pressure target of less than 130 mmHg as compared to a 130-149mmHg target. [11] Recent guidelines have drawn different conclusions from the evidence base, with the European guidelines recommending a target systolic blood pressure of 140mmHg (or higher) [12] and British guidelines a target of 130mmHg. [13]

In view of these controversies, the Prevention After Stroke- Blood Pressure (PAST-BP) study compared two different targets for blood pressure lowering after stroke or TIA in people recruited from a prevalent primary care population. [14] The aim was to determine whether setting a more intensive target in primary care would lead to a lower blood pressure, as a prelude to a trial powered to detect whether such a strategy would lead to a reduction in stroke recurrence.

**Methods**

Participants

The methods used in PAST-BP have been reported in detail elsewhere. [14] PAST-BP was an individually randomised trial in which participants were allocated either to an intensive blood pressure target (<130mmHg or a 10mmHg reduction if baseline pressure <140mmHg) or a standard target (<140 mmHg). Patients were recruited from 106 General Practices (of whom 99 contributed at least one patient) in England during 2009-2011. Patients were considered for inclusion if they were on the practice TIA/stroke register. They were excluded if: their baseline systolic blood pressure was less than 125 mmHg; they were already on 3 or more antihypertensives; they had >20mmHg postural change in systolic blood pressure on standing; they were already being treated to a 130mmHg systolic blood pressure target; they were unable to provide informed consent; or there was insufficient corroborative evidence that they had had a stroke or TIA. Potentially eligible participants were identified using a search of the General Practice clinical computer system. A general practitioner reviewed this list to exclude patients for whom a study invitation would be inappropriate. The remainder were sent a letter inviting them to attend a study clinic appointment held at their General Practice by a research nurse, where written informed consent was obtained. Ethical approval was provided by the Warwickshire Research Ethics Committee (reference 08/H1211/121).

Randomisation and masking

Randomisation was performed by the central study team at the University of Birmingham and was minimised on the basis of age, sex, diabetes mellitus, atrial fibrillation, baseline systolic blood pressure and general practice. Treatment allocation was ascertained by the research nurse either by telephone or online.

Neither participants nor clinicians were blinded to treatment allocation. The primary outcome measure (blood pressure) was obtained using automated sphygmomanometers and measured by a research nurse who was not otherwise involved in the patient's care.

Procedures

Patients randomised to the intensive arm were given a target systolic blood pressure < 130mmHg, or a target reduction of 10mmHg if their baseline blood pressure was between 125 and 140 mmHg. The target in the standard arm was <140 mmHg irrespective of baseline blood pressure. Apart from the different blood pressure targets, the management of blood pressure was the same in both groups, and was carried out by a practice nurse (to monitor blood pressure) and a General Practitioner (responsible for modifying blood pressure treatment). Patients whose systolic blood pressure at baseline was above target (everyone in the intensive arm, and those patients in the standard arm whose blood pressure was ≥140 mmHg) had their antihypertensive therapy reviewed by their General Practitioner. A practice nurse would see all patients at three month intervals (if their blood pressure was below target when previously measured) or at a one month interval (if previous blood pressure was above target), and refer to the general practitioner if the blood pressure was above target. No formal down-titration of therapy was required in the protocol if blood pressure was below target, but General Practitioners had discretion to change or reduce therapy in the light of symptoms attributable to blood pressure medication. General Practitioners were provided with treatment protocols that reflected the national guidelines for blood pressure lowering in operation at the time of the trial. [15] In both arms of the trial, the General Practitioners had access to a

computer based algorithm that actively suggested drugs and dosage if the participant was above target. Follow up ceased if the participant had a major cardiovascular event.

The primary outcome was change in systolic blood pressure between baseline and one year. Participants had blood pressure measured by a research nurse (separate from the practice nurse measurement described above) at baseline, six and twelve months. Blood pressure was measured using a British Hypertension Society validated automated electronic monitor supplied and validated for the study. [16] Blood pressure was measured in a standardised way, with the patient seated for five minutes and then six measurements taken at minute intervals. The primary outcome was the average of the second and third measurements.

Secondary measures of blood pressure included diastolic blood pressure at six and twelve months, systolic blood pressure at six months, and proportion achieving target blood pressures at twelve months. For the systolic blood pressure we also calculated the means of readings 2 to 6 and 5 to 6 to look for any differential effects with regard to habituation to blood pressure measurement.

Clinical events were identified through review of the general practice record at twelve months. These comprised: major cardiovascular events (composite of fatal and nonfatal stroke, myocardial infarction, fatal coronary heart disease or other cardiovascular death), emergency hospital admissions and deaths. Participants were flagged for mortality at the NHS Central Register. Side effects were assessed through the use of standard questionnaires. [14]

Statistical analysis

We estimated that a sample size of 305 patients in each group would detect a 5 mmHg difference in systolic blood pressure between groups with 90% power at a significant level of 5% assuming a standard deviation of 17.5 mmHg, 10% loss to follow up, 5% mortality and 10% major vascular events. [5,7] For the primary analysis, mixed models were used, adjusting for baseline blood pressure, age group (<80 years, ≥80 years), gender, diabetes mellitus, atrial fibrillation and practice (as a random effect). The principal analysis was a complete case analysis. We also explored the potential

effects of missing values by the use of three approaches: multiple imputation, group mean and by

last available value. Subgroup analyses were pre-specified for diabetes mellitus, atrial fibrillation

and age group. In addition, we performed a sub-group analysis by baseline systolic blood pressure

(<140mmHg, ≥140mmHg). The number of consultations, treatment changes and side effects were

compared using generalised mixed modelling, adjusting for the same variables as the primary

outcome. For clinical events, we calculated hazard ratios and their 95% confidence interval using Cox

proportional hazards modelling adjusting for the same covariates mentioned previously. We

checked the proportional hazard assumption with Schoenfeld residual plots and by including

interaction terms in the model (for each term by time). For all clinical event analyses, patients were

censored at the time of the first event relevant to that analysis. Thus, if a patient had more than one

emergency hospital admission, only the first one would be counted. Analysis was undertaken using

SAS 9.2 and Stata 12.


Patient involvement

The study was discussed by a stroke survivor group who agreed that it was an important research

question and that blood pressure was an important outcome for them. Patients were involved in

developing plans for recruitment and design of the study through representation on the Trial

Steering Committee. No patients were asked to advise on interpretation or writing up of the results.

We plan to disseminate the results of the research to the relevant patient community through local

and nationally organised stroke groups.


**Results**

Figure 1 shows the trial profile. 529 patients from 99 general practices (range 1 – 16 per practice)

entered the trial. 84 patients withdrew from the trial in the twelve months following randomisation

(52, 20% in the intensive target arm and 32, 12% in the standard target arm, p =0.02). Primary

outcome data were available for 379 participants at one year follow up (182, 68% in the intensive target arm and 197, 75% in the standard target arm). All patients were followed up for clinical events and deaths. Table 1 shows baseline patient characteristics. About a quarter of participants were on no blood pressure lowering treatment at randomisation (76 in intensive arm; 63 in standard arm). For half of participants, the index event was a TIA. Just under 20% of participants reported at least moderate disability (modified Rankin score of three or more). There were no important differences in characteristics between participants who did and did not have blood pressure recorded at twelve months (see table 1).

The intensive target arm was associated with significantly more consultations with the general practitioner and practice nurse for blood pressure control than the standard target arm (median visits 2 versus 1, p < 0.0001 and 3 versus 2, p = 0.002 respectively). This higher consultation rate led to more intensifications of blood pressure treatment (458 versus 278, p < 0.0001), and more changes due to side effects (77 versus 30, p < 0.0001). However, patients were also less likely to have their blood pressure treatment increased after review by the general practitioner when the blood pressure was above target in the intensive arm (109 versus 57, p = 0.005) (table 2). The three factors that contributed most to this difference were symptoms attributed to blood pressure medication, blood pressure only just above target, and patient not wanting treatment intensified. At the end of the study, the number of antihypertensive drugs that patients were on in both arms had increased by a similar amount (mean number of antihypertensive drugs 2.1 in intensive arm and 1.9 in standard arm, p = 0.13).

Treatment to a more intensive target was associated with a significantly greater reduction in systolic blood pressure at twelve months (primary outcome) (table 3). Systolic blood pressure was reduced by 16mmHg in the intensive target arm and by 13mmHg in the standard target arm. This difference persisted if it was calculated using the mean of the 5th and 6th reading: -3.2 mmHg, 95%CI -5.8 to -0.64) or the mean of the 2nd to 6th reading: -3.3mmHg, 95% CI -5.8 to -0.67) (see web appendix table i). Taking account of the missing values using multiple imputation the effect size was -3.2mmHg,

95% CI -5.7 to -0.65  (see web appendix table ii for results of other methods).   Blood pressure target

(i.e. < 130mmHg or a 10 mm Hg reduction for those with a baseline systolic blood pressure <

140mmHg) at one year was achieved in 93 (51.1%) patients in the intensive arm.  Proportions

achieving a systolic blood pressure < 140 mmHg were similar in the two arms (150/182, 82.4% versus

161/197, 81.7%, p = 0.59), as were those achieving a systolic blood pressure <130mmHg (103/182,

56.6% versus 107/197, 54.3%, p = 0.36). There was no evidence of a significant difference in

effectiveness of using an intensive blood pressure target in any patient sub-group (figure 2).

There was one major cardiovascular event in the intensive target arm (a non-fatal myocardial

infarction), and five in the standard care arm (3 strokes;  1 non-fatal myocardial infarction and 1

cardiovascular death) (HR 0.19, 95% CI 0.02 to 1.87, p = 0.16). There were two deaths in the

intensive target arm and one in the standard target arm. Risk of emergency admission was 12.8%

per annum in the intensive target arm and 7.8% per annum in the standard target arm (HR 1.56,

95%CI 0.84 to 2.93, p = 0.16).  Two admissions in each arm were related to falls. Apart from TIA

(responsible for five admissions in the standard target arm and three admissions in the intensive

target arm) and stroke, no single diagnosis accounted for more than two admissions.  Table 4 shows

the commonest symptoms at twelve months by treatment allocation. There were no significant

differences between the two groups.

**Discussion**

<u>Statement of principal findings</u>

We found that aiming for a target systolic blood pressure of <130 mmHg or 10mmHg reduction from

baseline if this was < 140 mmHg in a primary care population with prevalent cerebrovascular disease

led to a lower systolic blood pressure than if a <140 mmHg target was aimed for, but the difference

was small – about 3mmHg and was associated with increased workload – an extra consultation each

for GPs and nurses per year. The intensive target arm was not associated with more side effects as

measured at follow up, but there were more changes to treatment because of side effects during the trial. More people withdrew consent for the trial from the intensive target arm, and this might have reflected unwillingness to persevere with the increased medication regime. Perhaps the most important finding was the greater than 10mmHg reductions in mean systolic blood pressure in both arms of the study, so that over 80% of participants in each arm had achieved a blood pressure of < 140mmHg by the end of the trial, as compared to less than 50% at baseline.

Strengths and weaknesses of the study

Blood pressure at twelve months was not available for 28% of patients randomised. This reflected a high number of patient withdrawals from the study, with some differential loss to follow up in the intensive target arm. However, if missing values were imputed using multiple imputation – the most robust method -the difference in achieved blood pressure between arms at one year was very similar to that observed. Although we did not achieve our sample size, in the event our trial was adequately powered, since the observed standard deviation in blood pressure was less than we had anticipated in our sample size calculation. This is reflected in the statistical significance of the small difference in observed blood pressure between arms. Nevertheless, the upper limit of the confidence interval around the difference between arms at one year was 5.68mmHg, which would be regarded as a clinically important effect. Only 4% of patients on general practice stroke/TIA registers participated in the trial. Participants had a low prevalence of disability for a prevalent cerebrovascular disease population, were younger than typical patients in primary care with a history of cerebrovascular disease and over-represented people with a history of TIA only. [7] It is likely therefore that the more intensive target would have been even harder to achieve if the trial population was more representative of people with prevalent cerebrovascular disease. The trial represents a post-stroke primary care population managed by generalists rather than a selective hospital/ out-patient population managed by specialists. The outcome measure was unblinded, but

obtained using an automated sphygmomanometer by a nurse not directly involved in the participant's care, so systematic recording bias is unlikely.

The standard target arm in PAST-BP was actively managed, with support of a computer based algorithm that suggested medication changes rather than simply receiving 'usual care'. If we had used a more passive management strategy in the comparison group, we may have achieved a greater separation in systolic blood pressure between arms. In another blood pressure lowering study of patients with increased cardiovascular risk undertaken by our group in the same timeframe, the standard care control arm dropped by 6mmHg from a similar baseline compared to 13mmHg in the current study. [17] We used an active control as we wanted to ascertain the impact of setting different blood pressure targets, and to avoid confounding that would be introduced by having different management strategies in the two arms. The target in the intensive arm was more complicated than that in the standard care arm, but we minimised the impact of this on protocol adherence by ensuring that the primary care staff managed all trial participants in the same way, with prompts to review treatment if it was above the individualised target.

Comparison with other studies and interpretation

The change in mean blood pressure that we observed in the intensive target arm was very similar to that observed in the <130mmHg target arm of the SPS3 trial, with both PAST-BP and SPS3 achieving a mean systolic blood pressure in the intensive arm of 127 mmHg after one year. [11] However, the comparison arms had different achieved blood pressures (PAST-BP 129 mmHg versus SPS3 138 mmHg). This reflects the more conservative target in the higher target arm of SPS3 (130-149mmHg as opposed to <140mmHg), and that antihypertensive therapy was reduced if blood pressure fell below target.

Most of the observed reduction in blood pressure is likely to have been mediated by increased use of antihypertensive drugs, which on average went up from 1 to 2 drugs per person over the year of the study in both arms of the trial. Alternative explanations are that there was habituation to blood

pressure measurement leading to reduced white coat effect, or that there was regression dilution bias. However, in a blood pressure monitoring trial in a similar post-stroke population with similar mean baseline systolic blood pressure, no fall in blood pressure was observed in the control group over a twelve month period, [18] and in the SPS3 trial (also with similar mean baseline systolic blood pressure to PAST-BP) there was a fall of just 4 mmHg in the 140 mmHg target arm over the study period. [11] This suggests that the fall of 13 mmHg observed in the standard target arm of PAST-BP is unlikely to be primarily due to effects of regression dilution or habituation to measurement. Given that we had a relatively low systolic blood pressure inclusion criterion of ≥ 125 mmHg, important regression dilution bias would not be anticipated in this study.

Only 51% of patients in the intensive target arm of PAST-BP achieved their target blood pressure. Both patient wishes and general practitioner decision making led to treatment not being intensified when blood pressure was above target (table 2). Greater reluctance to lower blood pressure when near target, higher attribution of symptoms to blood pressure medication (table 2) despite an absence of objective evidence of increased symptoms (table 4) in the intensive target arm and greater reluctance of patients to increase treatment hint at the difficulties faced in achieving lower blood pressure targets in clinical practice. [19] This impression of practical difficulty is reinforced by the significantly higher proportion of participants that withdrew from the trial in the intensive arm. Although reported side effects and symptoms were similar in the two arms, and serious adverse events were infrequent (two admissions for falls in each arm), significantly more changes to treatment needed to be made because of side effects in the intensive target arm.


Implications

Recent evidence from SPRINT and a systematic review highlight the benefits of intensive blood pressure lowering. [20] [21] In some blood pressure target trials such as SPRINT and SPS3, the trial design maximised the achieved difference in blood pressure between the two arms, with the less intensive

arm having a target range rather than simply a < 140mmHg systolic target, and with treatment being reduced if blood pressure fell below the target range. This is an appropriate design for an explanatory trial designed to test the question does lowering blood pressure reduce risk of cardiovascular events? In our pragmatic trial which sought to test the effect of different blood pressure targets as they would be used in clinical practice, the protocol did not stipulate a reduction in blood pressure therapy if the blood pressure was below target and the control arm was actively managed to achieve a target blood pressure < 140mmHg.  As a result of this, and of reluctance on the part of both clinicians and patients to instigate all increases in blood pressure medication in the intensive group, the achieved difference in blood pressure between the two arms was small. Nevertheless, we found that active management was associated with clinically important reductions in blood pressure in both arms – the 13mmHg reduction achieved in the < 140mmHg arm equates to over 40% and 20% reduction in risk of stroke and coronary heart disease respectively. [22] Indeed, the reduction in blood pressure in our less intensive arm was similar to that achieved in the active arms of other blood pressure lowering trials and more than in their control groups. [11][17] The additional resources required to achieve the additional 3mmHg lower blood pressure in the intensive target arm might be better spent in increasing the proportion of people with stroke in primary care who have a systolic blood pressure < 140mmHg. Given this conclusion we did not feel that a pragmatic trial powered to detect a difference in cardiovascular end-points using an intensive target in primary care was warranted. Furthermore, the ongoing ESH-CHL SHOT trial will provide important data on whether intensive blood pressure lowering reduces cardiovascular events in people with stroke (who were excluded from the SPRINT trial). [23] The explanatory trial design is likely to lead to clear differences in achieved blood pressure in the treatment arms and confirm whether or not intensive blood pressure lowering reduces cardiovascular end-points in the post-stroke population.

*Panel: What this paper adds*

**What is already know on this subject**

- Lowering blood pressure after stroke is associated with lower risk of stroke recurrence, but there is uncertainty over what the target blood pressure should be

- One trial in people with recent lacunar stroke found that a systolic blood pressure target of < 130mmHg was associated with a non-significant reduction in stroke compared to a target of 130-149mmHg

- No trials have been carried out in primary care settings of different blood pressure targets after stroke

**What this study adds**

- Patients set a target of < 130mmHg or a 10mmHg reduction if initial blood pressure < 140mmHg achieved lower systolic blood pressures than those set a target of < 140mmHg, but the difference was small (3mmHg) in the context of the reduction in blood pressure observed in both arms (13mmHg and 16mmHg).

- Active management of blood pressure after stroke/TIA is more important than the target that is set.

Details of Contributors

Funding

Data sharing

No additional data available.

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**LEGEND FOR FIGURES**

**(Figures provided in separate file)**

**Figure 1: Trial profile**

‡ Reasons given: patient was housebound or in a nursing home (957, 33%); would be unable to provide consent (338, 12%); co-morbidity (216, 7%); blood pressure too low (199, 7%); at risk of falling (164, 6%); insufficient evidence of stroke/TIA (98, 3%); already being treated to 130 mmHg target (71, 2%); other patient factors (69, 2%); patient choice (54, 2%); terminally ill (48, 2%); deceased or left practice (41, 1%); participating in another trial (9). In 618 (21%) cases, no reason was given.

†blood pressure < 125mmHg 447; lack of corroborative evidence of stroke/TIA 60; on 3 or more antihypertensives 51; orthostatic hypotension 22; already being treated to lower BP target 4; unable to provide informed consent 2.

SBP: Systolic Blood Pressure

**Figure 2 Effect of intensive versus standard target on systolic BP at twelve months for different patient sub-groups**

Adjusted for baseline blood pressure, age group (<80, ≥80), gender, diabetes mellitus, atrial fibrillation and general practice (random effect)

|  | All participants | | Participants with systolic blood pressure recorded at 12 months | |
| --- | --- | --- | --- | --- |
|  | Intensive target | Standard target | Intensive target | Standard target |
|  | n=266 | n=263 | n=182 | n=197 |
| Age (years) | 71.9 (9.1) | 71.7 (9.4) | 72.6 (8.3) | 71.9 (9.5) |
| Men | 157 (59.0) | 156 (59.3) | 104 (57.2) | 125 (63.5) |
| White ethnicity | 260 (97.7) | 259 (98.5) | 180 (98.8) | 194 (98.5) |
| Current smoker | 25 (9.4) | 33 (12.6) | 15 (8.3) | 27 (13.9) |
| Systolic blood pressure | 142.9 (14.0) | 142.2 (13.4) | 143.5 (13.5) | 142.2 (12.9) |
| <140mmHg | 128 (48.1) | 129 (49.1) | 79 (43.4) | 98 (49.8) |
| >=140mmHg | 138 (51.9) | 134 (50.9) | 103 (56.6) | 99 (50.3) |
| Diastolic blood pressure | 79.9 (10.0) | 80.4 (9.8) | 78.8 (9.3) | 80.7 (10.1) |
| Diabetes mellitus | 26 (9.8) | 25 (9.5) | 19 (10.4) | 21 (10.7) |
| Atrial Fibrillation | 28 (10.5) | 27 (10.3) | 21 (11.5) | 22 (11.2) |
| Coronary heart disease | 41 (15.4) | 46 (17.5) | 28 (15.4) | 35 (17.8) |
| Chronic kidney disease | 26 (9.8) | 30 (11.4) | 19 (10.4) | 23 (11.7) |
| Heart failure | 2 (0.8) | 7 (2.7) | 1 (0.6) | 6 (3.1) |
| Peripheral vascular disease | 11 (4.1) | 11 (4.2) | 7 (3.9) | 6 (3.1) |
| Stroke | 130 (48.9) | 122 (46.4) | 85 (46.7) | 95 (48.2) |
| TIA only | 135 (50.8) | 141 (53.6) | 97 (53.3) | 102 (51.8) |
| Number of antihypertensive drugs | 1.0 (0.8) | 1.1 (0.8) | 1.1 (0.8) | 1.1 (0.8) |
| Number of other drugs | 4.5 (2.5) | 4.6 (2.6) | 4.5 (2.5) | 4.6 (2.6) |
| Total number of drugs | 5.6 (2.8) | 5.7 (2.7) | 5.6 (2.7) | 5.7 (2.7) |
| Modified Rankin scale† | | | | |
| 0 or 1 | 135 (50.8) | 125 (47.5) | 98 (53.8) | 84 (42.6) |
| 2 | 65 (24.4) | 69 (26.2) | 42 (23.1) | 57 (28.9) |
| 3 or 4 | 47 (17.7) | 51 (19.4) | 29 (15.9) | 42 (21.3) |

**Table 1: Baseline characteristics**

Data are mean (SD) or number (%); †Data missing for 19 patients in intensive arm and 18 in standard arm (all participants) and for 13 patients in intensive arm and 14 in standard arm (participants with 12 month systolic blood pressure).

|                                                                        | Intensive target (n=109) | Standard target (n=57) |
| ---------------------------------------------------------------------- | :----------------------: | :--------------------: |
| Other blood pressure readings (e.g. home readings) taken into account  | 17                       | 20                     |
| Patient did not want treatment intensified                             | 22                       | 13                     |
| Decision taken to re-measure blood pressure at future time             | 19                       | 12                     |
| Symptoms attributed to blood pressure medication                       | 24                       | 5                      |
| Blood pressure only just above target                                  | 14                       | 2                      |
| Patient had not been taking pills                                      | 9                        | 5                      |
| Blood pressure reading attributed to patient anxiety                   | 3                        | 8                      |
| Changes to drug therapy already made                                   | 4                        | 2                      |
| Postural hypotension                                                   | 3                        | 2                      |
| Awaiting specialist advice/ test results                               | 5                        | -                      |
| Intercurrent illness                                                   | 3                        | -                      |
| Patient too old for further increases in therapy                       | 1                        | 2                      |
| Change in lifestyle advocated rather than change in medication         | -                        | 1                      |

**Table 2: Reasons given by general practitioner for not increasing blood pressure medication after patient referred by practice nurse with blood pressure above target**

A reason was given for 164 of 166 non-intensification decisions. Numbers add up to more than 164 as in some cases two reasons were given.

|  | Mean blood pressure (mm Hg) | | | Mean difference from baseline (mm Hg) | | Effect size (mm Hg, 95% CI)† | |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Baseline | 6 months | 12 months | 6 months | 12 months | 6 months | 12 months |
| **Systolic blood pressure** | | | | | | | |
| Intensive target‡ | 143.5 (13.5) | 125.7 (14.5) | 127.4 (14.8) | -17.3 (16.7) | -16.1 (15.0) | -4.12 (-6.84 to -1.40) | -2.94 (-5.68 to -0.21) |
| Standard target* | 142.2 (12.9) | 129.3 (14.6) | 129.4 (14.8) | -12.7 (16.7) | -12.8 (17.2) | .. | .. |
| **Diastolic blood pressure** | | | | | | | |
| Intensive target‡ | 78.8 (9.3) | 73.1 (10.3) | 72.0 (9.0) | -6.5 (10.7) | -6.8 (9.1) | -1.14 (-2.86 to 0.58) | -1.63 (-3.10 to -0.15) |
| Standard target* | 80.7 (10.1) | 74.6 (9.8) | 74.4 (8.9) | -6.1 (9.7) | -6.3 (9.4) | .. | .. |

**Table 3: Systolic and diastolic blood pressure in intensive target and standard target groups**

Data are mean (standard deviation)

†Adjusted for baseline blood pressure, age group (<80, ≥80), gender, diabetes mellitus, atrial fibrillation and general practice (random effect)

‡Blood pressure data for 193 intensive target patients at six months and 182 at twelve months

*Blood pressure data for 198 standard target patients at six months and 197 at twelve months

|  | Intensive target arm | Standard target arm | Effect size Odds ratio (95% CI) | P value |
|---|---|---|---|---|
|  |  |  |  |  |
| Pain | 93/163 (57%) | 89/173 (51%) | 1.17 (0.75 to 1.84) | 0.48 |
| Breathlessness | 53/148 (36%) | 49/158 (31%) | 1.17 (0.72 to 1.92) | 0.53 |
| Fatigue | 75/149 (50%) | 88/163 (54%) | 0.81 (0.51 to 1.28) | 0.36 |
| Stiff joints | 93/162 (57%) | 99/176 (56%) | 0.94 (0.59 to 1.49) | 0.80 |
| Sore eyes | 35/148 (24%) | 24/158 (15%) | 1.68 (0.93 to 3.04) | 0.08 |
| Wheeziness | 32/163 (20%) | 28/175 (16%) | 1.24 (0.70 to 2.21) | 0.46 |
| Headaches | 27/151 (18%) | 36/165 (22%) | 0.69 (0.38 to 1.24) | 0.22 |
| Sleep difficulties | 56/150 (37%) | 66/163 (40%) | 0.81 (0.51 to 1.31) | 0.39 |
| Dizziness | 45/164 (27%) | 39/173 (23%) | 1.24 (0.74 to 2.08) | 0.42 |
| Loss of strength | 44/148 (30%) | 51/162 (31%) | 0.85 (0.51 to 1.40) | 0.52 |
| Loss of libido | 47/160 (29%) | 50/171 (29%) | 1.06 (0.65 to 1.72) | 0.83 |
| Impotence | 29/129 (22%) | 31/145 (21%) | 1.22 (0.65 to 2.30) | 0.54 |
| Pins and needles | 54/163 (33%) | 44/176 (25%) | 1.48 (0.91 to 2.41) | 0.11 |
| Cough | 40/144 (28%) | 49/160 (31%) | 0.86 (0.51 to 1.44) | 0.57 |
| Swelling of legs/ankles | 51/162 (31%) | 49/177 (28%) | 1.10 (0.67 to 1.81) | 0.70 |
| Dry mouth | 34/147 (23%) | 36/161 (22%) | 0.98 (0.57 to 1.70) | 0.95 |

**Table 4: Most frequent symptoms at 12 months**

Adjusted for baseline systolic blood pressure, age group (<80, ≥80), gender, diabetes mellitus, atrial fibrillation and general practice (random effect)
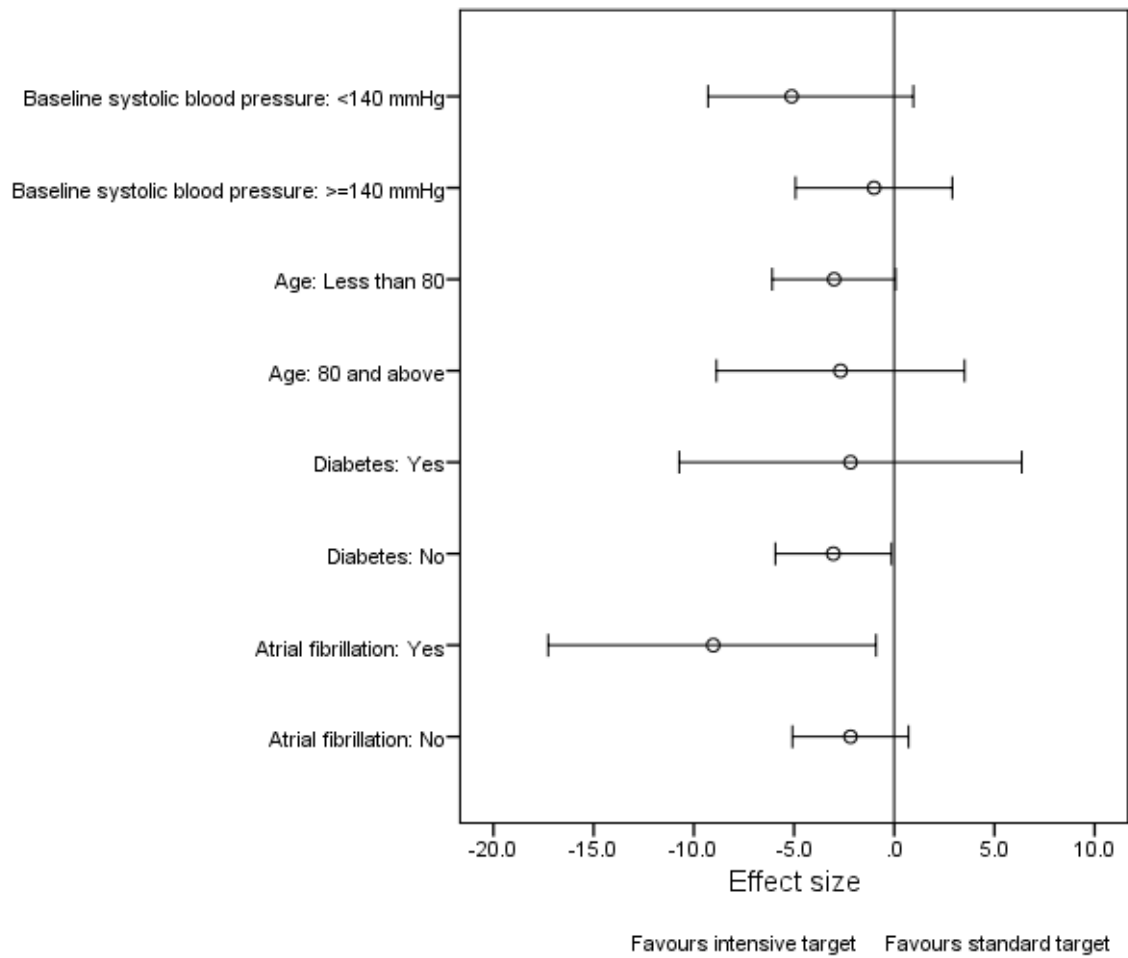
**Figure 2 Effect of intensive versus standard target on systolic BP at twelve months for different patient sub-groups**

Adjusted for baseline blood pressure, age group (<80, ≥80), gender, diabetes mellitus, atrial fibrillation and general practice (random effect)
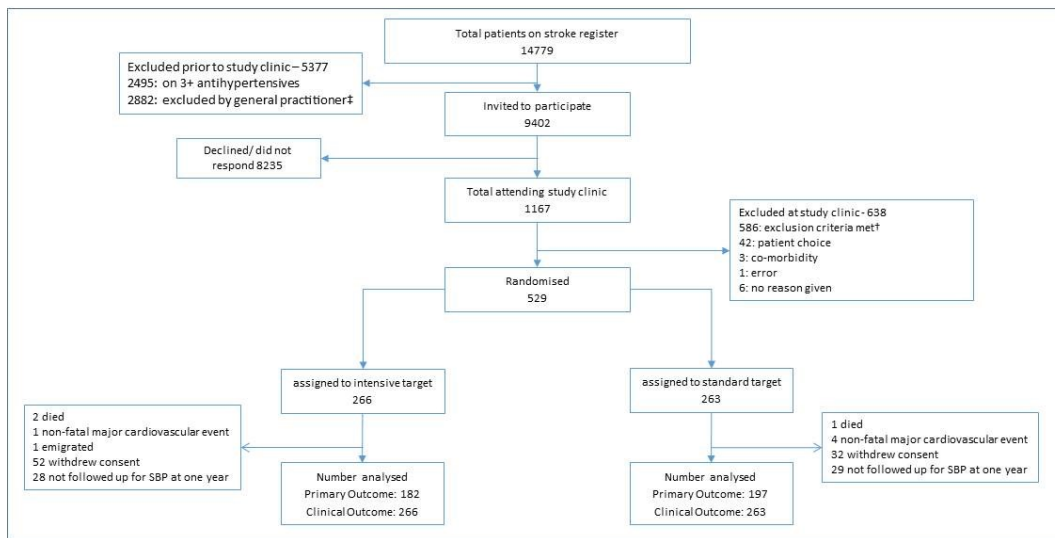
**Figure 1**