Effect of self-monitoring and medication self-titration on systolic blood pressure in hypertensive patients at high risk of cardiovascular disease

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Original Investigation

Effect of Self-monitoring and Medication Self-titration on Systolic Blood Pressure in Hypertensive Patients at High Risk of Cardiovascular Disease
The TASMIN-SR Randomized Clinical Trial

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IMPORTANCE Self-monitoring of blood pressure with self-titration of antihypertensives (self-management) results in lower blood pressure in patients with hypertension, but there are no data about patients in high-risk groups.

OBJECTIVE To determine the effect of self-monitoring with self-titration of antihypertensive medication compared with usual care on systolic blood pressure among patients with cardiovascular disease, diabetes, or chronic kidney disease.

DESIGN, SETTING, AND PATIENTS A primary care, unblinded, randomized clinical trial involving 552 patients who were aged at least 35 years with a history of stroke, coronary heart disease, diabetes, or chronic kidney disease and with baseline blood pressure of at least 130/80 mm Hg being treated at 59 UK primary care practices was conducted between March 2011 and January 2013.

INTERVENTIONS Self-monitoring of blood pressure combined with an individualized self-titration algorithm. During the study period, the office visit blood pressure measurement target was 130/80 mm Hg and the home measurement target was 120/75 mm Hg. Control patients received usual care consisting of seeing their health care clinician for routine blood pressure measurement and adjustment of medication if necessary.

MAIN OUTCOMES AND MEASURES The primary outcome was the difference in systolic blood pressure between intervention and control groups at the 12-month office visit.

RESULTS Primary outcome data were available from 450 patients (81%). The mean baseline blood pressure was 143.1/80.5 mm Hg in the intervention group and 143.6/79.5 mm Hg in the control group. After 12 months, the mean blood pressure had decreased to 128.2/73.8 mm Hg in the intervention group and to 137.8/76.3 mm Hg in the control group, a difference of 9.2 mm Hg (95% CI, 5.7-12.7) in systolic and 3.4 mm Hg (95% CI, 1.8-5.0) in diastolic blood pressure following correction for baseline blood pressure. Multiple imputation for missing values gave similar results: the mean baseline was 143.5/80.2 mm Hg in the intervention group vs 144.2/79.9 mm Hg in the control group, and at 12 months, the mean was 128.6/73.6 mm Hg in the intervention group vs 138.2/76.4 mm Hg in the control group, with a difference of 8.8 mm Hg (95% CI, 4.9-12.7) for systolic and 3.1 mm Hg (95% CI, 0.7-5.5) for diastolic blood pressure between groups. These results were comparable in all subgroups, without excessive adverse events.

CONCLUSIONS AND RELEVANCE Among patients with hypertension at high risk of cardiovascular disease, self-monitoring with self-titration of antihypertensive medication compared with usual care resulted in lower systolic blood pressure at 12 months.

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Elevated blood pressure is the leading risk factor for global disease burden.[1] Data from national and international surveys suggest that despite improvements over the last decade, significant proportions of patients have poor control of their elevated blood pressure.[2-5] Using the revised Eighth Joint National Committee (JNC 8) 2014 blood pressure guideline,[6] which proposed less restrictive targets for adults aged 60 years or older and for those with diabetes and chronic kidney disease, the proportion of adults in the United States with treatment-eligible hypertension who met blood pressure goals was less than half for younger adults (improved from 41.2% under JNC 7 to 47.5% under JNC 8 criteria) and less than two-thirds for older adults (although improved from 40% under JNC 7 to 65.8% under JNC 8).[7] Most management of hypertension is undertaken in primary care, where it comprises the most common long-term condition seen by family physicians, so it is appropriate that interventions are delivered in this setting.[8] Self-monitoring is now common, with approximately a third of patients with hypertension using it in the United Kingdom and more internationally.[9,10] Trials investigating self-monitoring have shown promise in the reduction of blood pressure particularly when combined with other interventions.[11]

The Telemonitoring and Self-Management in Hypertension 2 (TASMINH 2) trial found that self-management, comprising self-monitoring with self-titration of antihypertensives, resulted in significantly lower (5.4 mm Hg) systolic blood pressure after 1 year than did usual care.[12] However, the study included few patients with high-risk conditions such as cardiovascular disease, diabetes, or chronic kidney disease, in whom the blood pressure differences appeared to be smaller, suggesting the need for further investigation.

The potential advantage from optimal blood pressure control in patients at higher cardiovascular risk is large because the absolute benefit increases with absolute risk.[13] Guideline recommendations for blood pressure lowering vary for different high-risk groups.[6,14-18] At the time of protocol development for this study, the British Hypertension Society and other international guidelines had suggested a blood pressure target of less than 130/80 mm Hg for patients with stroke or transient ischemic attack, diabetes, stage 3 chronic kidney disease (without proteinuria), coronary heart disease, and myocardial infarction, providing uniformity across the range of high-risk groups.[14,19]

The aim of this trial was to determine whether self-management of hypertension resulted in lower blood pressure than usual care in a population of patients at high risk of cardiovascular events.

Methods

Study Design and Population

Targets and Self-Management for the Control of Blood Pressure in Stroke and at Risk Groups (TASMIN-SR) was a randomized unblinded trial with automated ascertainment of the primary end point. The trial methods have been described in detail elsewhere, but briefly, patients with a diagnostic Read code (clinical code) for at least 1 of the following: stroke or transient ischemic attack; diabetes; stage 3 chronic kidney disease (estimated glomerular filtration rate, 30-59 mL/min/m^2); coronary artery bypass graft surgery; myocardial infarction or angina with poorly controlled blood pressure (last recorded practice reading >145 mm Hg systolic) who were not under the care of a specialist were identified by their family physician using electronic searches of practice clinical record systems.[20] Family physicians reviewed the invitation list and excluded patients with terminal illness, patients who were house bound, or patients they otherwise believed to be unsuitable. The remaining potentially eligible participants were invited to their local clinic for a baseline examination conducted by the research team in conjunction with the Primary Care Research Networks in central and east England.[21]

To be eligible, patients had to be aged 35 years or older, have at least 1 of the high-risk conditions (cardiovascular disease, diabetes, stage 3 chronic kidney disease, or coronary heart disease), and have a blood pressure reading during the baseline examination of at least 130/80 mm Hg. Participants were not required to have been prescribed antihypertensive medication. Patients were excluded if they could not self-monitor because of dementia or if they had a score of more than 10 on the short-orientation memory concentration test; had blood pressure greater than 180/100 mm Hg; had postural hypotension, systolic blood pressure drop of more than 20 mm Hg; took more than 3 antihypertensive medications; were participating in another blood pressure study, had participated in TASMINH 2,[12] or had a spouse who had been randomized already in the current trial; had a terminal disease; were pregnant; were receiving care for their blood pressure by a specialist rather than by a primary care physician; or had experienced an acute cardiovascular event in the previous 3 months (**Figure 1**).

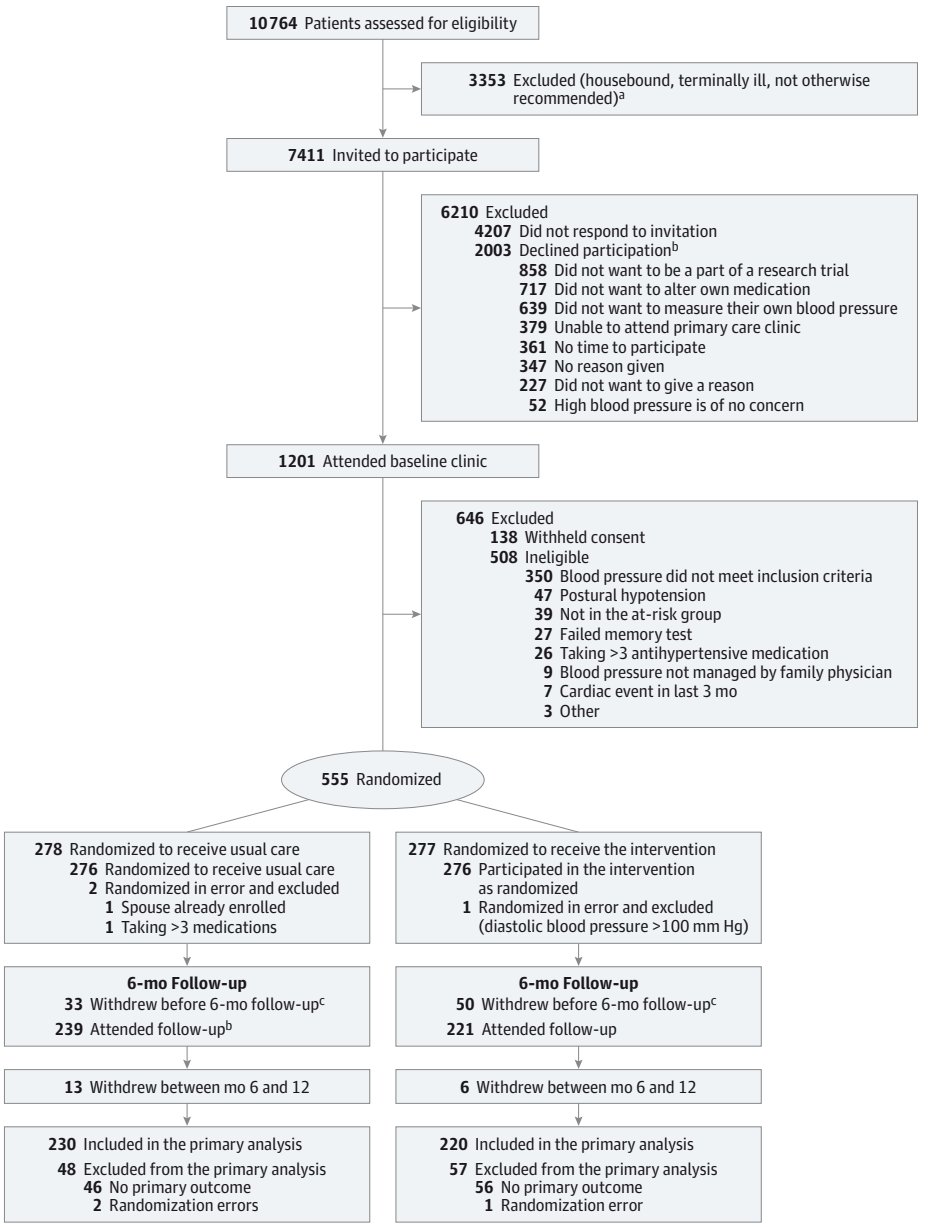
Approvals

Ethical approval was obtained from the North West—Greater Manchester East ethics committee (reference: 10/H1013/60) and site-specific research approval was obtained from the relevant primary care organizations.

Procedures

After hearing the explanation of the study and giving written informed consent, eligible patients were randomized between March and December 2011 using an Internet-based system with telephone backup to either usual care or self-management and were followed up for 1 year. Minimization, a method of adaptive stratified sampling that balances the different groups of clinical trials simultaneously for several factors, was used to balance treatment allocation by family practice, sex, age, high-risk group, and baseline systolic blood pressure, factors chosen due to their potential influence on systolic blood pressure.[22] One amendment was made following commencement of the study to allow reminder invitations to be sent to nonresponders. Patients randomized to usual care booked an appointment for a routine blood pressure check and medication review (including dose adjustment if required) with the participating family physician. Thereafter, blood pressure measurement, blood pressure targets, or adjustment of

Figure 1. Flow Through the Targets and Self-Management for the Control of Blood Pressure in Stroke and High-Risk Groups (TASMIN-SR) Trial



[a] The breakdown of reasons for exclusion is not known.

[b] Patients gave more than 1 answer.

[c] Two hundred thirty-nine of 243 patients in the control group attended the 6-month follow-up visit. Three were unable to be contacted and 1 had a serious illness in the family. Two hundred twenty-one of 226 patients in the intervention group attended the 6-month follow-up. Two were unable to attend due to illness and 1 had moved out of the area.

medication for patients receiving usual care were at the discretion of the family physician.

Patients randomized to self-management were trained to self-monitor blood pressure using a validated monitor (Microlife Watch BP Home[23]) with self-titration of medication following a predetermined plan, in 2 or 3 sessions, each lasting approximately an hour. Following training, intervention patients went to their family physician to agree with the individualized 3-step plan to increase or add antihypertensive medications. This was operationalized in a paper-based algorithm including the option for additional blood tests if required. Patients took their blood pressure twice each morning for the first week of each month using simple color-coded instructions developed for the TASMINH 2 trial.[12] Four or more blood pressure readings recorded during the measurement week for 2 consecutive months that were higher than the target necessitated a change in medication pursuant to the predetermined plan. Very high or very low readings (blood pressure >180/100 mm Hg or <100 mm Hg systolic, eFigure 1) required the participant to contact his/her practice. When a medication change was needed, patients sent a paper form to their family physicians without any need for a consultation. Medication choice remained at the discretion of the family physician. If patients used all 3 steps of their management plan, they returned to their general practitioner for additional instructions.

We selected blood pressure of less than 120/75 mm Hg as a target reading for the self-titration algorithms based on the British Hypertension Society (BHS)[9] and the Joint British Societies Guidelines[15] for patients with stroke or transient ischemic attack, diabetes (in the absence of proteinuria), chronic kidney disease, or coronary heart disease.

Outcomes

The primary prespecified outcome was the difference between intervention and control in systolic blood pressure at 12 months, taking into account baseline blood pressure and minimization factors. Patients attended 2 follow-up research clinics at 6 and 12 months after randomization. At both baseline and follow-up visits, blood pressure was measured by a research facilitator systematically after 5 minutes of rest using a validated electronic automated sphygmomanometer (Bp-TRU blood pressure M 100 or 200).[24] Six blood pressure readings were taken at 1-minute intervals. The mean of the second and third readings is considered to be best practice for obtaining a clinic blood pressure reading according to many international guidelines; therefore, this was used for the primary outcome. The main analysis was also rerun using the mean of the second to sixth blood pressure readings to reduce any influence of alerting effect to cuff inflation. Outcome ascertainment was not blind to allocation but was determined independently of the clinical team by a researcher using the automatic mode of the sphygmomanometer to measure the blood pressure without the need for intervention other than to place the cuff on the patient and switch on the monitor to reduce the potential for bias.

Other baseline clinical and questionnaire data were collected at the same clinics.[20] Prescribed medications were recorded from the electronic patient record with quality of life, anxiety, and adverse effects measured using standard questionnaires.[25-27] To allow comparisons of the amount of antihypertensive medications taken, individual drug doses were converted into defined daily doses (a World Health Organization–defined assumed average maintenance dose per day for a drug used for its main indication in adults).[28]

Statistical Analysis

Analyses were performed using STATA version 12 (StataCorp). A sample size of 243 patients per group was estimated for 90% power assuming a standard deviation of 17 mm Hg and a difference of at least 5 mm Hg in systolic blood pressure between intervention and control groups based on data from our previous trial.[12]

Assuming a 10% dropout rate during follow-up, a sample of 270 per group was required; a dropout rate of 20% would result in more than 85% power. The primary analysis included all participants who attended 12-month follow-up and had complete data for the primary outcome, without imputation. A mixed model was used to examine differences in between-group systolic blood pressure at 12 months, adjusting for baseline blood pressure, practice (as a random effect), sex, and high-risk group. Sensitivity analyses examined the potential effect of missing data including multiple imputation and replacement of missing data by the most recent previous data or by the mean of the series. For multiple imputation, 10 multiply-imputed data sets were generated using predictive mean-matching methods under the missing at random assumptions. Planned subgroup analyses were older vs younger (65 years as the threshold), men vs women, better controlled at baseline vs worse controlled at baseline (threshold, 145 mm Hg systolic), the different risk groups, and socioeconomic status.

Results

Of 10 764 potentially eligible patients from 59 family practices, 3353 were excluded by their family physician for being housebound, having a terminal illness, or not being thought suitable candidates. Of the remaining 7411 who were invited to participate, 1201 attended a baseline clinic and were assessed for eligibility. Of the 2003 who provided a reason for declining invitation (> 1 answer possible), 858 (43%) did not want to take part in a trial, 717 (36%) did not want to alter their own medication, and 639 (32%) did not want to measure their own blood pressure. Of the 646 patients who were excluded during the baseline examination, 350 (54%) had blood pressure readings that were not within the inclusion range and 138 (21%) withheld consent (Figure 1).

Of 555 patients randomized, 3 were randomized in error and were immediately excluded from the study, did not receive any intervention, and were not followed up or analyzed further. This left 276 patients in each group. After 12 months, 220 patients in the intervention group and 230 in the control group attended the final follow-up, providing 450 (81%) complete cases for analysis. Most who dropped out did so in the first 6 months (Figure 1). **Table 1** shows that the baseline characteristics of participants were well matched between groups. Participants for whom outcome data were not available were of similar age, had similar baseline blood pressure, but were less likely to be men (eTable 1 in Supplement 2).

The primary analysis plan specified adjusted results, but because these were very similar to the unadjusted results, the latter are presented for simplicity (see eTable 2 in Supplement 2 for adjusted results). After 12 months, there was a mean systolic blood pressure difference of 9.2 mm Hg (95% CI, 5.7-12.7) between the groups (**Table 2**). Multiple imputation for missing values showed a marginally lower mean difference in systolic blood pressure of 8.8 mm Hg (95% CI, 4.9-12.7). Further sensitivity analyses by the last observation carried forward or the mean of the series did not materially affect the primary outcome (eTable 3 in Supplement 2). The mean of the second to sixth blood pressure readings was almost identical to the primary analysis (mean difference in systolic blood pressure at 12 months, 9.1 mm Hg; 95% CI, 5.8-12.3; eTable 4 in Supplement 2).

After 6 months, there was a mean between-group systolic blood pressure difference of 6.1 mm Hg (95% CI, 2.9-9.3). There was also a mean between-group diastolic blood pressure difference of 3.0 mm Hg (95% CI, 1.4-4.7) at 6 months and 3.4 mm Hg (95% CI, 1.8-5.1) at 12 months (Table 2). After multiple imputation the point estimates were slightly lower: the mean systolic between-group difference at 6 months was 5.5 mm Hg (95% CI, 1.6-9.5) and the mean diastolic difference was

2.7 mm Hg (95% CI, 0.4-5.1) at 6 months and 3.1 mm Hg (95% CI, 0.7-5.5) at 12 months. There were no significant differences in the primary outcome within any of the prespecified subgroups (**Figure 2**).

Prescription of antihypertensive drugs increased in both groups but significantly more in the intervention group: the mean defined daily doses at 12 months for the intervention group was 3.34 (95% CI, 3.1, 3.7) vs 2.61 (95% CI, 2.4-2.9) for the control group (mean difference, 0.9; 95% CI, 0.7-1.2; **Table 3**, adjusted results are presented in eTable 5 in Supplement 2). Comparison with the number of drug classes prescribed shows that this represents both an increase in dose and in the number of medications. The main changes seen were in the prescription of calcium channel blockers, and thiazides, which significantly increased in the intervention group compared with the control group (Table 3).

Although reported adverse symptoms were common in both groups (**Table 4**), there were no significant differences between control and intervention groups. Additional symptoms that could be linked to antihypertensive treatment were not significantly different between groups including dizziness, impotence, and rash. Two patients in the control group were admitted to the hospital with chest pain, 1 on 3 occasions; 3 had transient ischemic attacks; and 1 had a possible stroke. In the intervention group, 3 patients were admitted to the hospital with chest pain, 2 were admitted with arrhythmias, and 4 had transient ischemic attacks. One control patient and 1 intervention patient died during the study; neither death was judged to be study related.

There were no significant differences between groups in quality of life measured by the EQ-5D at 6 or 12 months (eTable 6 in Supplement 2).

Table 1. Unadjusted Baseline Characteristics of 552 Patients Randomized

	Usual Care (n = 276)[a]	Intervention (n = 276)[a]
Age, mean (SD), y	69.6 (9.7)	69.3 (9.3)
Men, No. (%)	164 (59.4)	166 (60.1)
Blood pressure, mean (SD), mm Hg		
Systolic	144.2 (13.9)	143.5 (12.8)
Diastolic	79.9 (9.4)	80.2 (9.7)
Race, No. (%)		
White	267 (96.7)	266 (96.4)
Black	3 (1.1)	5 (1.8)
Asian	5 (1.8)	3 (1.1)
Other	1 (0.4)	2 (0.7)
Body mass index, mean (SD)[b]	30.5 (5.7)	30.2 (5.0)
No. of patients	271	266
Married, No. (%)	193 (69.9)	210 (76.1)
Level of education, No. (%)		
Degree or higher	34 (12.3)	30 (10.9)
School or professional certification	150 (54.4)	162 (58.7)
No qualification/not known	92 (33.3)	84 (30.4)
Occupation, No. (%)		
Professional/managerial and technical	124 (44.9)	134 (48.6)
Skilled manual and nonmanual	95 (34.4)	87 (31.5)
Partly skilled and unskilled	22 (8.0)	30 (10.9)
Unemployed, unwaged, or unknown	35 (12.7)	25 (9.1)
Index of Multiple Deprivation (2007), mean (SD)[c]	16.5 (11.7)	17.4 (13.6)
Current smoker, No. (%)	19 (6.9)	17 (6.2)
Anxiety score (STAI-6), mean (SD)[d]	(n = 264) 13.9 (2.2)	(n = 270) 13.7 (2.2)
Past medical history, No. (%)		
Coronary heart disease	83 (30.1)	85 (30.8)
Cerebrovascular disease	48 (17.4)	52 (18.8)
Diabetes	128 (46.4)	123 (44.6)
Chronic kidney disease	90 (32.6)	86 (31.2)
≥ Relevant comorbidities, No. (%)[e]	60 (21.7)	59 (21.4)
Defined daily dose, mean (SD)[f]	2.4 (1.8)	2.2 (1.7)

[a] Number of participants unless otherwise stated. Three patients (2 usual care, 1 intervention) were randomized in error and are excluded from this table (see Figure 1).

[b] Calculated as weight in kilograms divided by height in meters squared.

[c] Index of Multiple Deprivation 2007: median for English Primary Care Trusts 23.6 with higher scores reflecting greater deprivation.

[d] State Trait Anxiety Inventory 6 (STAI-6; range 6-24, high scores reflect greater anxiety) correlates with longer form Spielberger state anxiety inventory for which an adult norm adjusted to the same scale would be 10.5.[26]

[e] Two or more from the 4 groups above.

[f] Defined daily dose as classified by World Health Organization. Figures combine standardized "average maintenance dose" and number of medications.[28]

Discussion

This trial has shown for the first time, to our knowledge, that a group of high-risk individuals, with hypertension and significant cardiovascular comorbidity, are able to self-monitor and self-titrate antihypertensive treatment following a prespecified algorithm developed with their family physician and that in doing so, they achieved a clinically significant reduction in systolic and diastolic blood pressure without an increase in adverse events. These results were sustained and increasing during the 12 months of the trial. Based on systematic reviews of clinical outcome trials,[13] the blood pressure difference observed in those self-managing would be expected to be associated with an approximate 30% reduction in stroke risk should it be sustained.[12,13]

In terms of weaknesses, the follow-up of patients in the trial was not as high as hoped. Nevertheless, primary outcome data were available on more than 80% of participants, and differences in blood pressure between groups were similar whether or not missing data were accounted for in the sensitivity analyses. Given that the trial population had significant comorbidity, it is to be expected that loss to follow-up would be higher than in a hypertensive population without these comorbidities. Those lost to follow-up were more likely to be men (especially in the intervention group). Recruitment took place in 59 family practices over a wide geographical area and hence logistics were complex. Most of the dropout occurred between baseline and 6 months, particularly in the intervention group, which may have reflected patients who felt unable to continue in the trial once exposed to the intervention.

Table 2. Unadjusted Systolic and Diastolic Blood Pressure in Intervention and Usual Care Groups

	Blood Pressure, mm Hg							
	Baseline		6 Month		12 Month		Difference[b]	
	No. of Patients	Mean (95% CI)[a]	No. of Patients	Mean (95% CI)[a]	No. of Patients	Mean (95% CI)[a]	6 Month	12 Month
Systolic Blood Pressure Complete Case								
Usual care	230	143.6 (141.9-145.4)	225[c]	138.1 (136.0-140.3)	230	137.8 (135.4-140.3)	6.1 (2.9-9.3)	9.2 (5.7-12.7)
Intervention	220	143.1 (141.4-144.9)	215	131.8 (129.6-134.1)	220	128.2 (125.9-130.4)		
Systolic Blood Pressure With Multiple Imputation for Missing Values								
Usual care	276	144.2 (142.3-146.1)	276	138.4 (136.3-140.5)	276	138.2 (136.1-140.2)	5.5 (1.6-9.5)	8.8 (4.9-12.7)
Intervention	276	143.5 (141.6-145.4)	276	132.1 (129.8-134.4)	276	128.6 (126.5-130.7)		
Diastolic Blood Pressure Complete Case								
Usual care	230	79.5 (78.3-80.8)	225[c]	77.2 (75.9-78.5)	230	76.3 (75.0-77.6)	3.0 (1.4-4.7)	3.4 (1.8-5.1)
Intervention	220	80.5 (79.2-81.8)	215	75.3 (74.0-76.6)	220	73.8 (72.6-75.0)		
Diastolic Blood Pressure With Multiple Imputation for Missing Values[a]								
Usual care	276	79.9 (78.8-81.1)	276	77.6 (76.4-78.8)	276	76.4 (75.1-77.7)	2.7 (0.4-5.1)	3.1 (0.7-5.5)
Intervention	276	80.2 (79.1-81.4)	276	75.2 (73.9-76.4)	276	73.6 (72.4-74.8)		

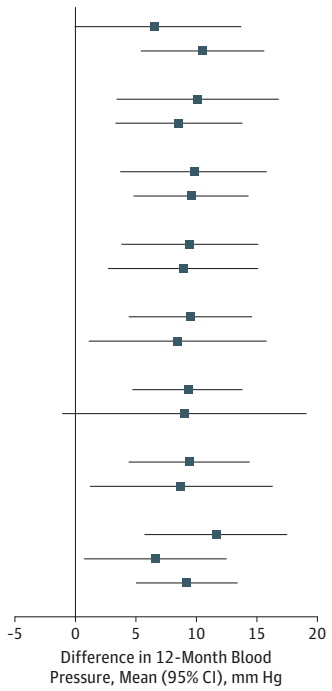
[a] Mean of second and third blood pressure readings.

[b] Blood pressure difference between intervention and usual care groups taking into account baseline difference.

[c] Blood pressure data unavailable for one person who attended sixth month follow-up.

Figure 2. Blood Pressure Difference at 12 Months by Subgroup for Systolic Blood Pressure

	No. of Patients	Difference in 12-Month Blood Pressure, Mean (95% CI), mm Hg[a]	Subgroup Comparison *P* Value
Age, y			
≤65	149	6.5 (-0.7 to 13.7)	.37
>65	301	10.5 (5.4 to 15.6)	
Sex			
Women	174	10.1 (3.4 to 16.8)	.72
Men	276	8.5 (4.1 to 13.0)	
Blood pressure systolic			
>145	173	9.8 (3.7 to 15.8)	.96
≤145	277	9.6 (4.8 to 14.3)	
Diabetes			
Absent	246	9.4 (3.8 to 15.1)	.91
Present	204	8.9 (3.7 to 14.1)	
Chronic kidney disease			
Absent	304	9.5 (4.4 to 14.6)	.82
Present	146	8.4 (1.1 to 15.8)	
Stroke or transient ischemic attack			
Absent	373	9.3 (4.7 to 13.8)	.96
Present	77	8.9 (-1.1 to 19.1)	
Coronary heart disease			
Absent	311	9.4 (4.4 to 14.4)	.88
Present	139	8.7 (1.2 to 16.3)	
IMD2007[b]			
Lower	225	11.6 (5.7 to 17.5)	.24
Higher	225	6.6 (0.7 to 12.5)	
Overall		9.2 (5.0 to 13.4)	



[a] The difference in blood pressure between groups at 12 months accounts for baseline blood pressure.

[b] IMD indicates the index of multiple deprivation. Higher values correspond to worse deprivation.

Table 3. Unadjusted Prescription of Antihypertensives (Number and Defined Daily Dose) in Intervention and Usual Care Groups[a]

	Time Point						Difference Between Intervention and Control	
	Baseline		6 Month		12 Month			
	No. of Patients	Mean (95% CI)	No. of Patients	Mean (95% CI)	No. of Patients	Mean (95% CI)	6 Month	12 Month
No. of Antihypertensive Drugs								
Usual care	230	1.63 (1.46 to 1.79)	226	1.75 (1.58 to 1.92)	230	1.73 (1.56 to 1.91)	0.19 (−0.01 to 0.39)	0.27 (0.07 to 0.47)
Intervention	220	1.59 (1.42 to 1.76)	215	2.07 (1.87 to 2.26)	220	2.22 (2.03 to 2.42)		
Overall Defined Daily Dose								
Usual care	230	2.34 (2.10 to 2.58)	226	2.57 (2.33 to 2.81)	230	2.61 (2.37 to 2.85)	0.66 (0.17 to 1.15)	0.91 (0.42 to 1.40)
Intervention	220	2.16 (1.91 to 2.40)	215	3.05 (2.80 to 3.30)	220	3.34 (3.09 to 3.59)		
Defined Daily Dose Thiazides								
Usual care	230	0.23 (0.17 to 0.29)	226	0.24 (0.18 to 0.30)	230	0.23 (0.17 to 0.29)	0.11 (0.02 to 0.24)	0.16 (0.04 to 0.29)
Intervention	220	0.23 (0.17 to 0.30)	215	0.35 (0.29 to 0.42)	220	0.39 (0.33 to 0.46)		
Defined Daily Dose Calcium Channel Blockers								
Usual care	230	0.43 (0.33 to 0.53)	226	0.52 (0.42 to 0.62)	230	0.55 (0.44 to 0.65)	0.23 (0.03 to 0.44)	0.28 (0.08 to 0.49)
Intervention	220	0.46 (0.36 to 0.57)	215	0.79 (0.68 to 0.89)	220	0.86 (0.75 to 0.96)		
Defined Daily Dose Angiotensin-Converting Enzyme Inhibitor/Angiotensin II Receptor Blockers								
Control		1.42 (1.24 to 1.60)	226	1.55 (1.37 to 1.73)	230	1.59 (1.41 to 1.77)	0.26 (−0.11 to 0.62)	0.34 (−0.02 to 0.70)
Intervention		1.22 (1.04 to 1.41)	215	1.61 (1.43 to 1.80)	220	1.74 (1.55 to 1.92)		
Defined Daily Dose β-Blockers								
Usual care	230	0.15 (0.11 to 0.19)	226	0.15 (0.11 to 0.19)	230	0.14 (0.10 to 0.18)	0.03 (−0.05 to 0.11)	0.02 (−0.06 to 0.09)
Intervention	220	0.14 (0.10 to 0.18)	215	0.17 (0.13 to 0.21	220	0.15 (0.11 to 0.19)		

[a] Defined daily dose as classified by World Health Organization. Figures combine standardized "average maintenance dose" and number of medications.[28]

Included patients were mostly white, from a professional or skilled manual background, and were prescribed 3 or fewer antihypertensives, which might limit generalizability. Randomized groups were similar with small differences in comorbidities in favor of the intervention group. No difference in blood pressure reduction from the intervention was seen between the subgroups examined, but this may reflect inadequate statistical power. Any practice effects were taken into account in the randomization and method of analysis. Individual randomization and dropouts from the intervention group could have caused contamination between the groups, but this would have biased the results toward no effect. Similarly, high-performing practices taking part in research would have also mitigated against the observed effect.

Relatively small proportions of those potentially eligible to take part were eventually randomized. Family physicians could exclude patients from invitation to the trial who were housebound, had terminal illness, or who were thought to be unsuitable, which is likely to have included frailer patients. Nevertheless, those included were older (mean age 70 years) and had more comorbidities than our previous work (22% had 2 or more strokes, coronary heart disease, diabetes or chronic kidney disease). As with TASMINH 2, only approximately 8% of those invited to take part were randomized. Responses from more than 2000 of those who declined suggest that nonresponse reflected a combination of not wishing to take part in a trial and not wishing to self-manage. More than double the number randomized were prepared to self-manage as measured by those attending eligibility screening, and of those excluded, controlled blood pressure was the commonest reason. Taken together, for patients outside of a trial situation, we estimate that the intervention might be suitable for about 20%. The study was unblinded but ascertainment of outcome was by automated sphygmomanometer, which did not require research facilitator input other than to fit the cuff to the patient and switch on the monitor. The potential for the intervention group to become habituated to blood pressure measurement was lessened by the use of the BP-TRU monitor (which takes 6 readings at a time) for all study end points in both randomization groups and the fact that the primary outcome was almost identical whether the mean of the second and third or second to sixth blood pressure readings was used.

Patients in the intervention group were using home targets based on the then recommended clinic target of 130/80 mm Hg for all 4 groups.[17,19] In the intervening years, target recommendations have tended to roll back toward 140/90 mm Hg or higher for most conditions although UK stroke guidelines and those for diabetes in the presence of renal disease remain equivalent

Table 4. The 10 Most Frequently Reported Adverse Effects Plus Selected Hypertension Medication–Specific Symptoms or Adverse Effects at 12 Months

	No. (%) of Patients		
	Usual Care (n = 230)	Intervention (n = 220)	*P* Value
Stiff joints	110 (48)	109 (50)	.72
Pain	113 (49)	101 (46)	.49
Fatigue	106 (46)	93 (42)	.42
Swelling of legs and ankles	78 (34)	81 (37)	.52
Sleep difficulties	86 (37)	71 (32)	.26
Breathlessness	66 (29)	68 (31)	.61
Dry mouth	74 (32)	58 (26)	.18
Cough	65 (28)	64 (29)	.85
Pins and needles	61 (27)	52 (24)	.48
Loss of libido	49 (21)	48 (22)	.90
Additional hypertension medication specific symptoms			
Dizziness	43 (19	53 (24)	.16
Impotence	36 (16)	37 (17)	.74
Rash	23 (10)	18 (8)	.50

to those used in the trial.[14] Patients in the control group received usual care without specification of target, which may have accentuated the difference between groups given that the achieved mean blood pressure in the control group was 138/76 mm Hg.

Three previous trials have considered self-monitoring with self-titration of antihypertensives.[12,29,30] Two trials, including our previous study, showed reduction of blood pressure through self-monitoring with self-titration.[12,29] The third, which used a cluster design, found that a web-based self-titration intervention increased blood pressure monitoring but did not affect blood pressure.[30]

The current study achieved a greater blood pressure reduction than seen previously and seems to have been mediated through greater use of medication in the intervention representing both an increase in dose and in number of antihypertensive medications. Increases were particularly observed in the use of thiazide diuretics and calcium channel blockers comprising a difference of almost 1 defined daily dose between randomized groups.[28] Adherence to study medication—difficult to ascertain accurately and typically high in studies such as this—was not measured, but the observed difference of 9 mm Hg systolic blood pressure seen between groups is what would be expected for this degree of medication intensification.[13,31]

A recently published systematic review found no other self-titration trials but showed a range of blood pressure reductions from interventions combining self-monitoring with additional support compared with usual care in other high-quality trials.[11] For these studies at the 12-month follow-up, there was consistent benefit with a mean net reduction in both systolic blood pressure (range, −2.1 to −8.3 mm Hg), diastolic blood pressure (range, 0.0 to −4.4 mm Hg), or both. The blood pressure differences from the current study are at the upper end of these values and broadly equivalent to that achieved in other trials of self-monitoring combined with behavioral self-management or a web-based intervention and additional pharmacist care.[32,33]

Conclusions

This study has shown that self-monitoring with self-titration of antihypertensives is feasible and achievable in a high-risk population without special equipment and by following a modest amount of training and additional family physician input. This is a population with the most to gain in terms of reducing future cardiovascular events from optimized blood pressure control. Furthermore, despite the significantly reduced blood pressure, no additional adverse events were observed. Validated semiautomated blood pressure monitors are now widely available, costing as little as US $25 (£15, €18), meaning that with training delivered by nurses, this intervention could be implemented widely. At least 30% of patients with hypertension are already self-monitoring in the United Kingdom and more internationally,[10] and there is a significant prevalence of comorbidities,[34] suggesting that self-management could be appropriate for many individuals, notwithstanding the issues discussed concerning generalizability.

Among hypertensive patients at high risk of cardiovascular disease, self-monitoring with self-titration of antihypertensive medication, compared with usual care, resulted in lower systolic blood pressure at 12 months. Patients at high risk of cardiovascular disease whose blood pressure is not optimally controlled could be considered for self-management.

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