Systematic Review: Does self-monitoring reduce blood pressure? Meta-analysis with meta regression of randomised controlled trials.

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Does self monitoring reduce blood pressure? Meta-analysis with meta regression of randomised controlled trials.

Running Title: Meta-analysis of blood pressure self monitoring

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Abstract short version

Introduction: Self monitoring of blood pressure (BP) is an increasingly common part of hypertension management. The objectives of this systematic review were to evaluate the systolic and diastolic BP reduction, and achievement of target BP, associated with self monitoring.

Methods: Medline and six other databases were searched for studies where the intervention included self monitoring of BP and the outcome was change in office/ambulatory BP or proportion with controlled BP. Two reviewers independently extracted data. Meta analysis using a random effects model was combined with meta-regression to investigate heterogeneity in effect sizes.

Results: 25 eligible RCTs were identified. Office systolic and diastolic BP were significantly reduced in those who self-monitored compared to usual care (weighted mean difference systolic: -3.82mmHg (95 % CI -5.61, -2.03) /diastolic -1.45 mmHg (-1.95, -0.94)). Self monitoring increased the chance of meeting office BP targets (RR = 1.09 (1.02, 1.16)). There was significant heterogeneity between studies for all three comparisons which could be partially accounted for by the use of additional co-interventions. Mean daytime ambulatory blood pressure was not significantly reduced by self monitoring.

Conclusion: Self-monitoring reduces blood pressure by a small but significant amount. Meta-regression could only account for part of the observed heterogeneity.

Keywords: Blood Pressure Monitoring, Hypertension, Meta-analysis, Self-Monitoring

Key messages:

1) Self-monitoring of blood pressure results in small reductions in office blood pressure but there is significant heterogeneity of results between studies
2) Metaregression to investigate this heterogeneity found that additional co-interventions such as telemonitoring or education explained part but not all of the heterogeneity in studies with achievement of blood pressure target as their outcome.
3) Other factors not studied may play an important role in the remaining heterogeneity and may be best studied by an individual patient meta-analysis.

Abbreviations

mmHg; Millimetres of Mercury

BP; Blood Pressure

RCT(s); Randomised Controlled Trial(s)

SBP: systolic Blood Pressure

DBP: Diastolic Blood Pressure

WMD; Weighted Mean Difference

ABPM: Ambulatory Blood Pressure Measurement

RR: Relative Risk

Introduction

Hypertension is a key risk factor for cardiovascular disease, the leading cause of death worldwide.[1] Therapeutic reduction of blood pressure leads to significant reduction in both stroke and coronary heart disease risk and is cost effective, especially for individuals at higher risk of cardiovascular events.[2, 3] However, international community based surveys indicate that only a minority of people treated for hypertension are controlled to recommended treatment levels.[4]

Self monitoring of hypertension has been proposed as a method for reducing blood pressure over and above standard care by increasing the involvement of individuals in their own treatment and therefore aiming to increase adherence, reduce clinical inertia and provide patients and professionals with common information about the efficacy of treatment.[5, 6] Self measurement is a better predictor of end organ damage than office measurement [7] and is well tolerated by patients.[8, 9]

Previous systematic reviews have found self monitoring of blood pressure to be associated with lower office systolic blood pressure (around 4 mmHg) as compared to conventional care but also found large variation in effect size with significant heterogeneity between studies.[5, 10] No reviews have reported the effect of self monitoring using ambulatory blood pressure as the outcome. The heterogeneity previously reported may reflect the substantial variation in a number of key variables such as the study setting, the methodologies employed (e.g., length of follow-up, measurement of BP (how, when and by whom), co-interventions, the BP definitions utilised), and the classification criteria for home, self, and usual care. Since these previous meta-analyses were performed, a number of new trials have

been published. The aim of this study was therefore to provide an updated systematic review of the evidence for self monitoring in hypertension and to explore any heterogeneity found using meta regression. The objectives were to determine the effect of self monitoring of blood pressure in adults on blood pressure and blood pressure control, compared to usual care (no self monitoring of BP). The outcomes used were office and ambulatory systolic and diastolic blood pressure, and number of patients meeting office target blood pressure. [The protocol for this review can be found in appendix 1 (include as web appendix)].

Methods

Searching

Electronic databases (Medline, Embase, Cochrane database of systematic reviews, database of abstracts of clinical effectiveness, the health technology assessment database, the NHS economic evaluation database, and the TRIP database) were searched in February 2009 for articles published up to and including January 2009, using a search strategy (Appendix 2) based on those used in previous meta-analyses which was designed to capture all randomised controlled trials (RCTs) concerning self monitoring and self management of hypertension.[5, 10] Additionally, reference lists from included studies and previous meta-analyses were searched. Reference titles and abstracts of publications resulting from the search were scrutinised independently by two reviewers and potentially eligible studies reviewed in detail to assess eligibility.

Selection

RCTs were eligible if the intervention tested included self measurement of BP without medical professional input and if a blood pressure outcome measure was available that had been taken independently of the self measurement (either systolic or diastolic office pressure or ambulatory monitoring (mean day time ambulatory pressure)). Non randomised designs were excluded. No additional quality criteria in terms of methodology or study size were applied.[11]

Data extraction

Data were extracted independently using a coding form [included as web appendix 3] by two reviewers (RM and EB) concerning patient characteristics (gender, age), study characteristics (length of follow up), type of self monitoring (home, community), co-interventions (any procedure over and above self monitoring that was included in the intervention including patient education, nurse led support, telemonitoring), and outcomes (see below). Where data were missing from published reports, for instance standard deviations of change, authors were contacted to request such information. Where studies reported more than one outcome time (e.g. 6 and 12 months), data concerning the longest follow up was extracted. In cases of disagreement that could not be resolved by consensus, a third reviewer (JM) adjudicated.

Outcomes

The outcomes assessed were change in mean office SBP and DBP, change in mean day-time ambulatory SBP and DBP between baseline and follow up for both intervention and control arms, and change in proportion of people with office measured BP controlled below target

between intervention and control arms. Data were also collected on whether adjustments were made for self-monitored readings compared to office readings.

Quantitative data synthesis

Analyses were performed with STATA 10.1 (Statacorp) using a random-effects model (metan command). Weighted mean differences (WMD) were calculated for the overall mean change in systolic and diastolic blood pressure (both office and ABPM) between intervention and control, with relative risk (RR) used when percentage of patients with BP above target at final follow-up was reported. The weighting depended on the standard deviation of the change in BP from baseline to final reading and this value was not always reported but standard deviations at baseline and final measurements were given. Elementary theory of differences of correlated variables was used to estimate the standard deviation of change on those occasions. The correlation between baseline and final result was estimated from studies where all three standard deviations were reported and then used in conjunction with the latter two standard deviations to estimate the standard deviation of change when not available. Where either of the latter two standard deviations were missing then an average value from the other studies was imputed. [The data used and an explanation of the standard deviation estimation can be found in web appendix 4].

Clinical heterogeneity was assessed using a chi-square test for systematic variation and I^2. Heterogeneity was further explored using meta-regression with backward elimination to analyse the associations between treatment effect and the study characteristics (metareg command). Where a significant moderator of the heterogeneity was found, studies were grouped using this moderator and if heterogeneity of effect size persisted with respect to

blood pressure change, further meta regression was performed within groups. A priori, on the basis of results from previous studies suggesting an effect on outcome, we included terms for age (continuous) and sex of participants,[12, 13] length of follow up (continuous),[6] use of additional co-interventions (where these were part of the intervention in addition to self monitoring),[10] adjustment made for self-monitored BP readings, and inclusion criteria for diastolic blood pressure (DBP of ≥90 v ≥95 mmHg) in the regression models.[5] Meta-regression was not used for the ambulatory BP outcome, due to the small number of studies involved. A series of sensitivity analyses were performed to assess the impact of each study on the overall outcome with recalculation of both the weighted mean differences and meta regression as each study was removed one at a time from the analysis. A specific sensitivity analysis considered whether studies with multiple arms influenced the degree of heterogeneity as measured by I^2.

Results

The search results are presented in Figure 1. Of 630 studies included in the original search results, 25 studies including 27 comparisons were eligible for the meta analysis (Table 1). Two studies included three arms and so were included twice.[14, 15] Of these, 20 RCTs (21 comparisons, 5898 patients) contained extractable data on change in office systolic blood pressure, 23 RCTs (25 comparisons, 6038 patients) data for change in office diastolic blood pressure, 12 RCTs, (13 comparisons, 2260 patients) data for achievement of office blood pressure target and three studies for change in mean day time ambulatory BP (SBP and DBP) (3 comparisons, 572 patients).

Nine studies included follow up of one year or more and the mean age of participants ranged from 47 to 77 with 18 studies having a mean age of less than 60 (table 1). Six studies included 200 or more patients per randomised group. Thirteen studies included no additional intervention other than self monitoring. Additional co-interventions over and above self monitoring included patient education (7 studies), phone contact or home visits (7 studies), family involvement (1 study) and telemetry (6 studies). Seven studies included more than one additional co-intervention. The treating physician was aware of self blood pressure readings in 16 studies.

Office Systolic Blood Pressure

Systolic blood pressure was significantly reduced in those who received self-monitoring compared to usual care (weighted mean difference = -3.82mmHg, (95 % CI -5.61 to -2.03) Figure 2). However, there was a high level of heterogeneity between the studies (I^2 = 71.9%, p<.001). Subsequent meta-regression demonstrated that of the six variables investigated as moderators for this heterogeneity, none approached significance.

Sensitivity analyses, which examined the influence of each individual study on the overall effect size estimate by removing each study in turn from the analysis, revealed a range of weighted mean differences of between -3.14 and -4.11 mmHg, with no single study affecting the overall heterogeneity. In particular the Green study which was included twice did not have any distorting effect.

Office Diastolic Blood pressure

Diastolic blood pressure was significantly reduced in those who received self-monitoring compared to usual care (weighted mean difference = -1.45mmHg (95 % CI -1.95 to -0.94), Figure 3). Again, there was significant (albeit this time moderate) heterogeneity between the studies (I^2 = 42.1%, p<0.01). Meta-regression demonstrated that none of the six variables investigated as moderators approached significance.

The range of weighted mean differences seen in the sensitivity analysis removing each study in turn from the analysis was between -1.23 and -1.62 mmHg. On five occasions, removing a single included study had an effect on the resultant meta-analyses and meta-regressions of the remaining studies: with Haynes[16] removed gender approached significance as a moderator (p=0.075); with Binstock,[17] Green (a),[14] Parati[18] and Marquez-Contreras[19] removed, co-interventions approached significance as a moderator (p=0.056, p=0.069, p = 0.05, p=0.091, respectively). In each case, meta analyses on the remaining studies split by whether or not they contained an additional co-intervention, were now homogenous and showed that the presence of a co-intervention resulted in approximately double the effect size. A sensitivity analysis of the two trials included twice examining their effect on z scores and I^2 was consistent with the magnitude of the individual effect sizes and suggested no distortion caused by including both arms of these trials.

Office Target Blood Pressure

Self monitoring of blood pressure (12 RCTs, 13 comparisons) increased the chance of meeting target compared to usual care (relative risk = 1.09 (95% CI 1.02 to 1.16), Figure 4). There was significant heterogeneity between the studies (I^2 = 76.3%, p <.01) which was moderated by the presence of a co-intervention (z = 2.43, p<0.02) in the meta-regression.

Where self monitoring was accompanied by an additional co-intervention, participants were more likely to meet target BP compared to where there was none (RR = 1.34, (95% CI 1.2 to 1.51), vs RR = 0.98, (95% CI 0.91 to 1.05)). However, none of the other included moderators could explain the heterogeneity which remained in both groups.

Sensitivity analyses showed that removing each study individually made little difference to the overall relative risk (range 0.97 to 1.03). None of these analyses affected the remaining heterogeneity in the relative risk.

Fewer than half of the studies reported achievement of target blood pressure as an outcome. To determine if there was bias related to choice of outcome, the SBP and DBP office analyses were re-run including only those studies that also reported target BP. These analyses had little impact on the overall effect size (SBP WMD = -3.2mmHg (95% CI -5.65 to -0.75), DBP WMD = -1.45mmHg (95% CI -2.57 to -0.47)) suggesting little if any bias in terms of chosen outcome for the target analysis.

Day-time Ambulatory Blood Pressure

Mean day-time ambulatory blood pressure was reduced but not significantly in those who received self-monitoring compared to usual care (three studies, weighted mean difference = SBP: -2.04mmHg (95 % CI -4.35 to 0.27), I^2 <0.05%, p=0.89 figure 5a, and DBP: -0.79mmHg (95% CI -2.35 to .77), I^2 <0.05% p=0.96), figure 5b). The I^2 suggested homogeneity but has limited power with only three studies. Sensitivity analyses removing each study in turn showed that the Parati study (which included telemonitoring)[18] had the greatest effect

altering the WMD by about 0.5 mmHg in both the SBP and DBP analyses. However, none of these analyses altered the non-significant nature of the results. An analysis for target ambulatory BP was not undertaken as these data were only reported in the Parati study.

Publication Bias

Funnel plots [see web appendix 5] imply several unpublished negative studies may exist but that these are likely to have small (<100) sample sizes and thus little effect on the overall results.

Discussion

This review has found that self monitoring has a small but significant effect on blood pressure control: As with previous meta-analyses, significant heterogeneity was apparent between all studies with office blood pressure as the outcome.[5, 10] Meta-regression to investigate this heterogeneity was not explanatory for the comparisons with office blood pressure as an outcome but sensitivity analyses considering office diastolic pressure showed that five studies individually influenced this heterogeneity. In four cases absence of these studies resulted in co-interventions becoming a significant moderator of this heterogeneity. In the case of the target blood pressure analysis, meta-regression showed that studies including additional co-interventions were more likely to result in blood pressure control and that this explained some but not all of the heterogeneity. Where ambulatory blood pressure was the end point, a smaller and non significant reduction in daytime ambulatory blood pressure was observed. This may reflect a lack of power with only three studies included.

This meta-analysis, unlike previous work, provides some explanation of the heterogeneity observed between studies, particularly in terms of the co-interventions used.[5, 10] The range of co-interventions utilised in the included trials was wide and included patient education, health professional support (phone calls, pharmacist involvement, additional clinic visits or home visits), patient led drug titration, techniques designed to increase medication compliance, and use of a website and telemonitoring with automated feedback. It is perhaps unsurprising that these could enhance the effect of self monitoring given that multi faceted interventions are more likely to result in improvements in outcome, and this was seen definitively in the target blood pressure analysis.[20]

Blood pressure drops with repeated measurement,[21] and it has been previously suggested that habituation to measurement might be the mode of action of self monitoring. The smaller effect size seen in the ambulatory monitoring analysis provides some support for this argument, but included only three studies hence should be interpreted with caution.[18, 22, 23] Furthermore, if habituation had a large effect it might have been expected that the length of study would have moderated some of the heterogeneity in the meta regression, but this was not observed.

The recent scientific statement from the American Heart Association, American Society for Hypertension and Preventive Cardiovascular Nurses Association recommends that the target self blood pressure goal for treatment is <135/85mmHg or <130/80mmHg in high-risk patients.[24] The evidence underlying these recommendations is not robust: the majority of trials included in this meta-analyses report target “office blood pressure” of 140/85-95 mmHg but many do not explicitly state whether the same target levels were applied to the

self monitoring. The importance of this can be seen from the results from the THOP trial where the same target was used for both self and office measurements and it was found that basing treatment decisions on self readings led to higher blood pressures than basing them on office readings.[25]

The current paper includes more than double the number of patients in previous meta-analyses and has resulted in a reduction in the point estimates of effect size for both systolic and diastolic blood pressure. The relatively small effect of self monitoring is likely to result in a lack of power in most included studies (only one of which had enough patients to detect a 3mmHg difference between groups). This fact, along with the evidence from the funnel plots, increases the possibility of unpublished negative studies such as has been postulated previously.[5]

Despite a range of potential moderators chosen *a priori* to explore the heterogeneity between studies including age, sex, length of follow up, and inclusion diastolic blood pressure, observed heterogeneity remained largely unexplained by this analysis which suggests that other factors may play a role. Possibilities which might be further investigated include: the timing of self monitored readings (variation of blood pressure during the day may impact on patient's perceptions of their BP), the setting of self monitoring (home, at a GP surgery or in the community), and changes in treatment during the study. Further work should also explore the types of co-interventions and how differing combinations of these might optimise the impact on reducing BP and helping patients reach target levels. This might best be done in an individual patient data meta analysis.

Conclusion

Self monitoring of blood pressure has a small but significant effect on reduction of office blood pressure when compared to usual care. Co-interventions explain part of the observed heterogeneity between studies which used achievement of target blood pressure as an outcome but most remains unaccounted for. Future investigators should consider carefully the design of their intervention and the use of outcomes such as ambulatory monitoring that are less likely to be affected by habituation to blood pressure measurement.

Contributorship

EB, RM and JM performed the searches and extracted the data. EB, RM and RH performed the analyses. All authors participated in the writing of the final document and approved the final version. RM will act as guarantor for the study.

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Competing interests

The authors declare that they have no competing interests regarding this paper

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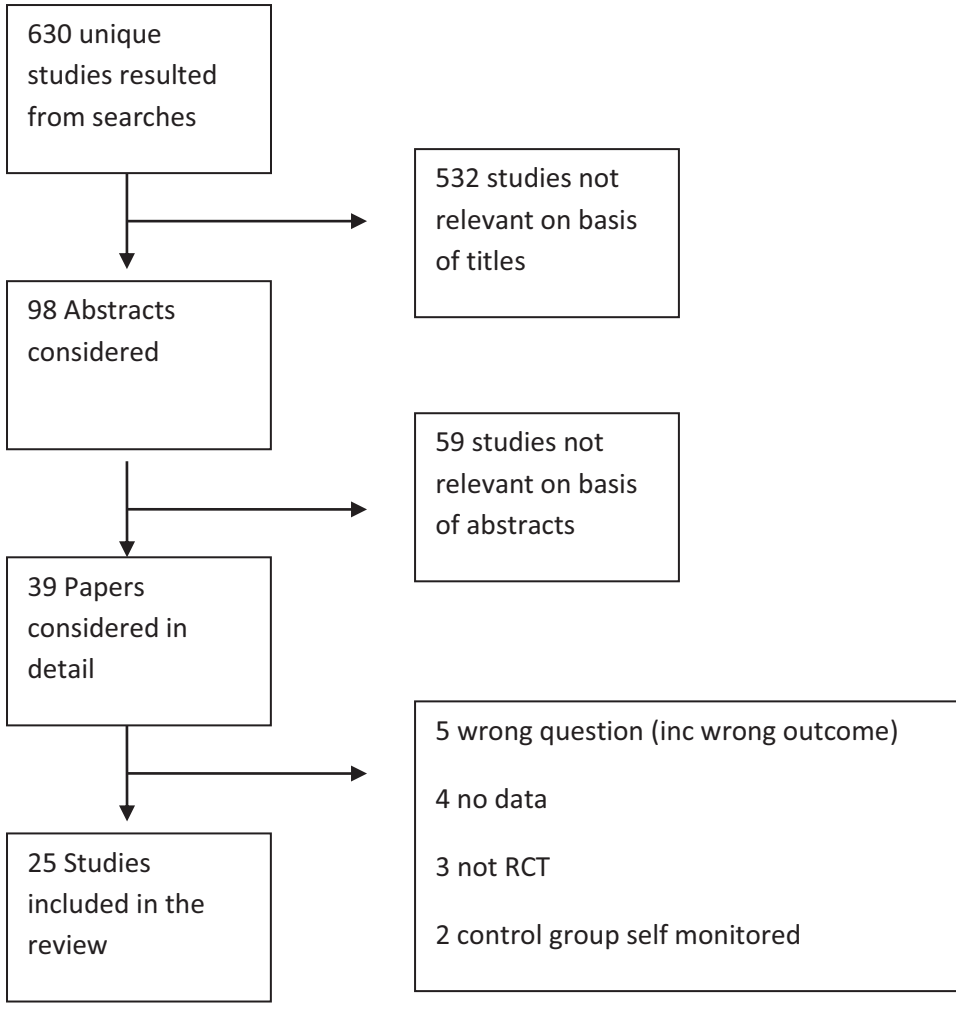

Figure 1 Flow chart of search results

Figure 2: Overall Office Systolic BP results

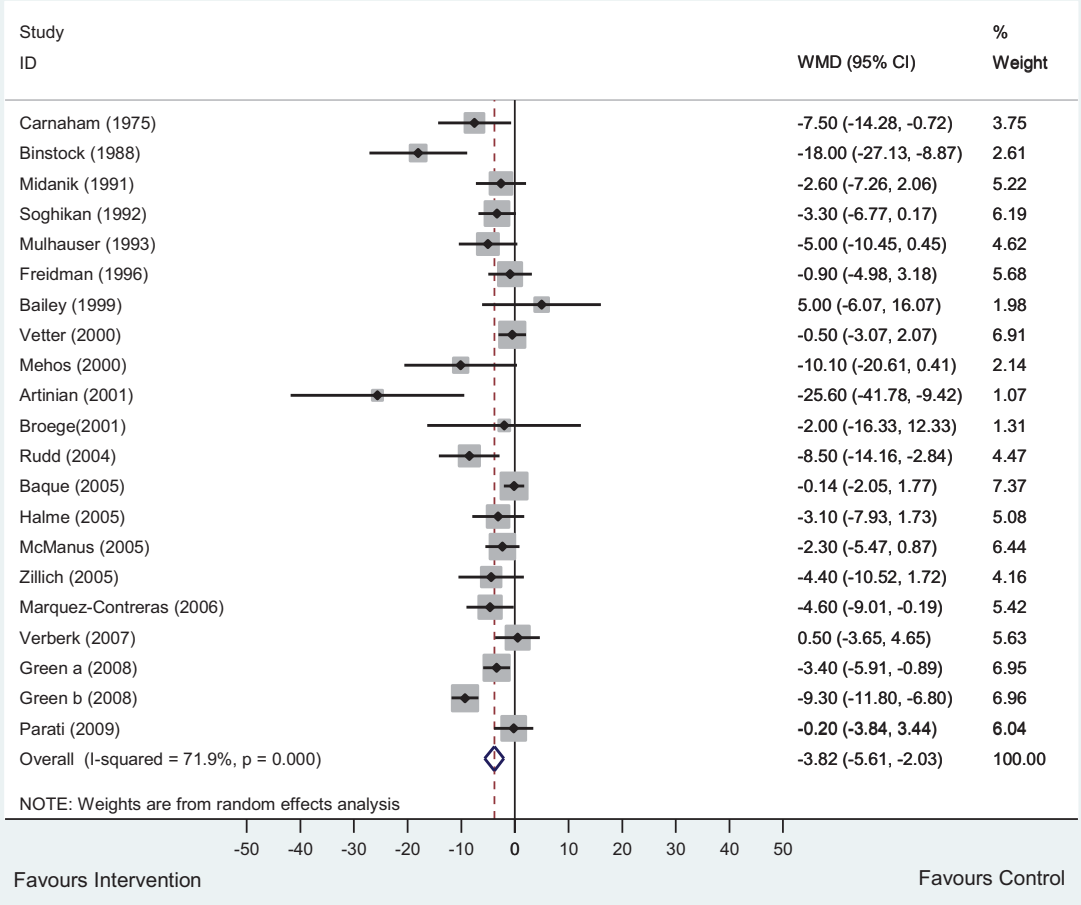

Figure 3:Overall Office Diastolic BP results

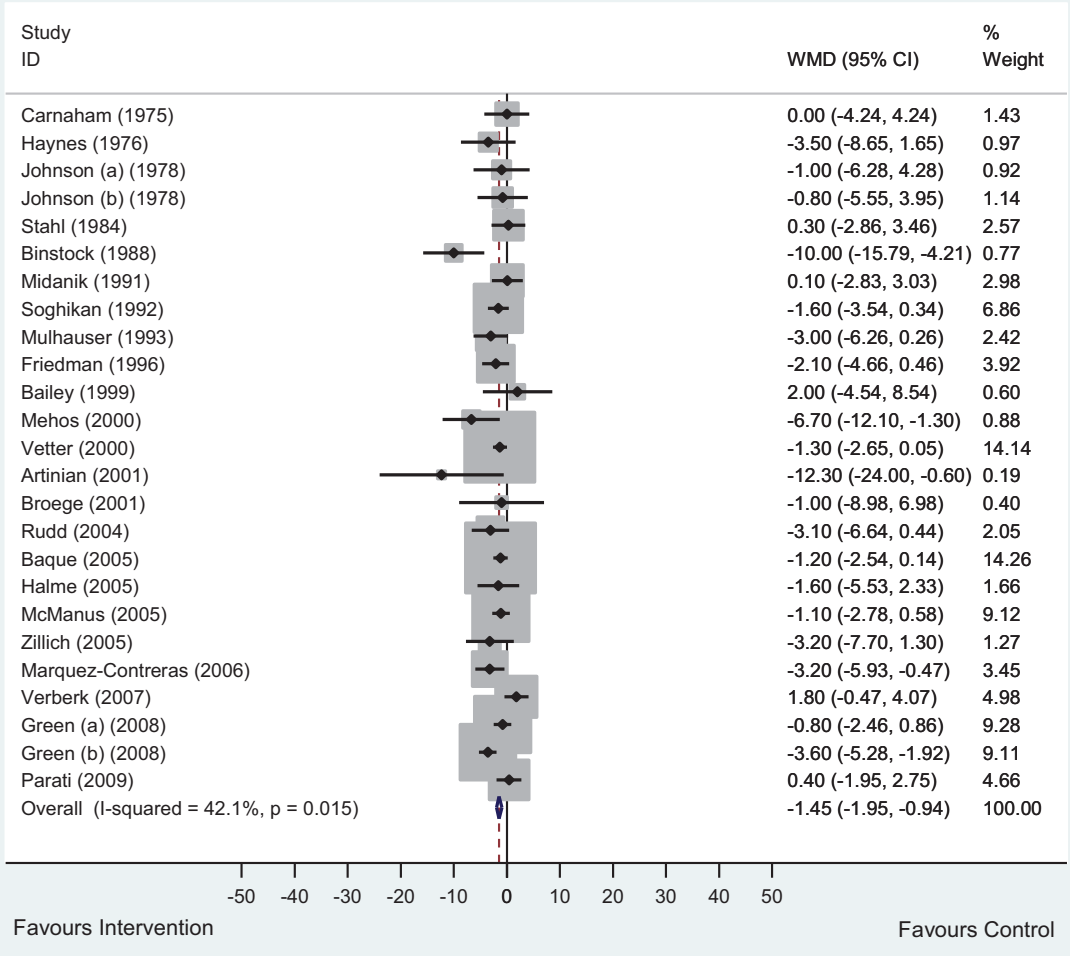

Figure 4: Office Target BP results

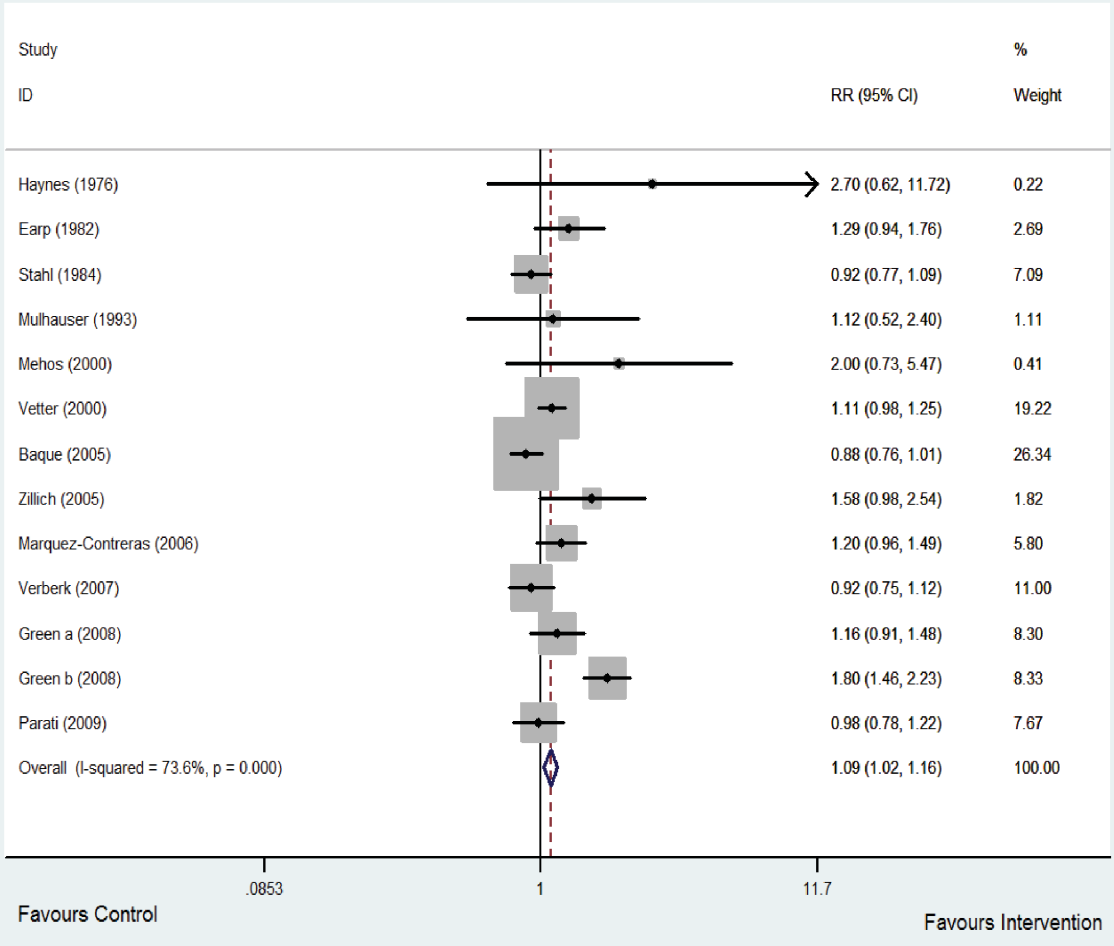

Figure 5a: Daytime Ambulatory SBP results

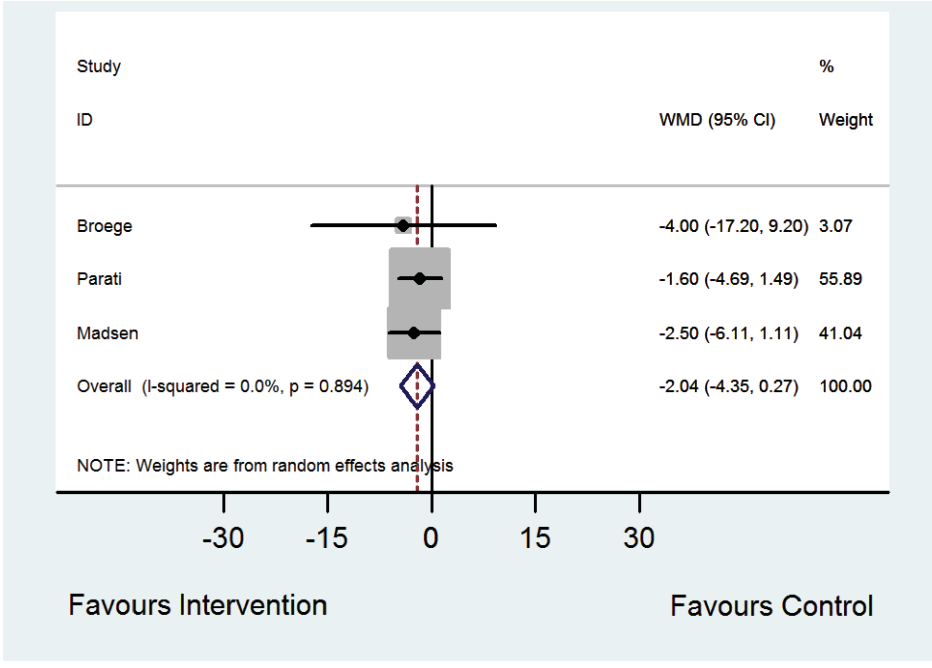

Figure 5b: Daytime Ambulatory DBP results

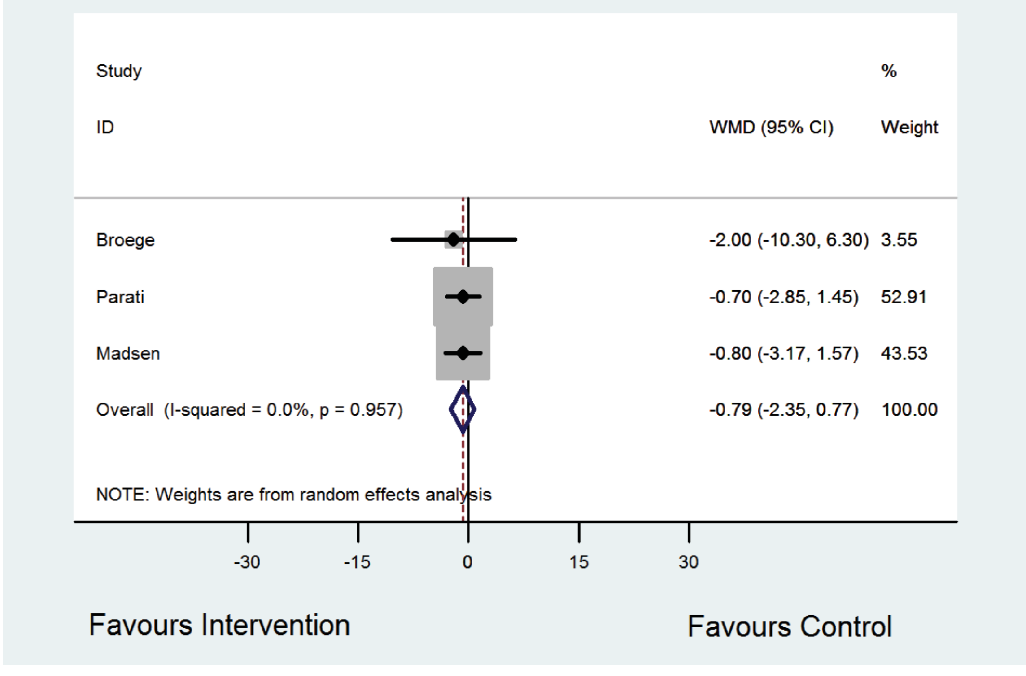

Table 1 Summary of randomised studies of self monitoring of blood pressure

Study	Setting and subjects	Mean Age (years)	Intervention subjects	Control Subjects	Length of follow up	Type & frequency of BP self measurement	Description of the control group	Intervention group regimen over and above control plus self-monitoring	Adjustment made for self-measurement readings	Was physician adjusting medication aware of self measurement readings?	Outcome measurement
Carnahan 1975 US [26]	Hospital clinic, patients starting treatment for hypertension, with DBP≥90	55	49	48	2-8 clinic visits per 6 months	Manual sphyg with built in stethoscope Twice daily (upper arm)	Medication adjustment by fixed titration schedule based on clinic BP values done by nurse	No additional co-intervention	None specified	No: Nurse run clinic blind to home BP	Clinic BP (blinded) Compliance (pill count)
Haynes 1976 US [16]	Non compliant men recruited via workplace screening programme; DBP ≥ 90mmHg following initial treatment	No age quoted	20	18	0 & 6 months	Manual anaeroid Daily (upper arm)	Not specified	Patient education and tailored to their rituals	None specified	Not clear	Blinded external BP measurement
Johnson a * 1978 Canada [15]	Subjects recruited from screening in local shopping centre, DBP ≥95 mmHg despite treatment	54	36	36	0, 2wks, & 6 months	Manual sphyg Daily (upper arm)	Neither home visits or self-recording	No additional co-intervention	None specified	Yes	External blinded measurement of BP and compliance (pill count & interview)

Study	Setting and subjects	Mean Age (years)	Intervention subjects	Control Subjects	Length of follow up	Type & frequency of BP self measurement	Description of the control group	Intervention group regimen over and above control plus self-monitoring	Adjustment made for self-measurement readings	Was physician adjusting medication aware of self measurement readings?	Outcome measurement
Earp 1982 US [27]	Treated hypertensives with a medication change in previous 2 mths recruited from hospital and community clinics	48	99	63	24 months; 5-6 visits	Sphygmomanometer type unclear	Routine medical care	Home visit and significant others involved	None specified	Not clear	DBP control
Stahl 1984 US [28]	Hospital clinic. Raised DBP under care of nurse practitioner	47.5	144	173	36 months, variable number of visits	Mercury Sphyg	Not specified	No additional co-intervention	None specified	yes	Unblinded physician measured
Binstock 1988 US [17]	Treated hypertensives	Not stated	23	32	0 & 12 months	Not stated. Readings done at home	Education programme	educational programme plus self-monitoring	None specified	Not stated	Change in SBP and DBP
Midanik 1991 US [29]	Untreated with BL DBP 90-95mmHg and SBP< 180mmHg	47	102	102	0 & 12 months	Digital device. 2 consecutive readings, twice a week	Usual care	No additional co-intervention	None specified	Yes	Change in SBP and DBP
Soghikhan 1992 US [12]	Health Maintenance Organisation Centres. Hypertension patients	54	215	215	0 & 12 months	Electronic sphyg Twice weekly	Usual care	No additional co-intervention	None specified	Yes	Study BP by trained technicians (blinded)

Study	Setting and subjects	Mean Age (years)	Intervention subjects	Control Subjects	Length of follow up	Type & frequency of BP self measurement	Description of the control group	Intervention group regimen over and above control plus self-monitoring	Adjustment made for self-measurement readings	Was physician adjusting medication aware of self measurement readings?	Outcome measurement
Muhlhauser # 1993 Germany [30]	Primary Care. BP> 160 and/or 95mmHg	51	86	74	0 & 18 months	Twice daily until satisfactory values achieved then less frequently	Normal care	Patient education	None specified	Yes	Hypertensive prescription, Physician visits
Friedman 1996 US [31]	Community physicians' clinics. Treated hypertensives with SBP ≥ 160mmHg and/or DBP ≥ 90mmHg	77	133	134	0 & 6 months	Automated Weekly (?upper arm)	Usual care	Patient education and telemetry	None specified	"TLC" data transmitted to patient's own physician	BP measured on home visit; protocol for measurement not clear if blinded
Bailey 1999 Australia [32]	Primary care. Hypertensive patients not practising self-measurement, with or without current treatment	55	31	29	0 & 8 weeks	Electronic Twice daily (upper arm)	ACE inhibitor or diuretic	No additional co-intervention	None specified	Yes	Externally measured BP (study nurse). Probably not blinded
Vetter 2000 Switzerland [33]	Primary care. Newly diagnosied or known hypertensives with BP 160/200/ 95-215mmHg	58	296	326	0, 2 & 8 weeks	Automated (wrist) Twice daily	Losartan 15mg	No additional co-intervention	None specified	Not applicable (patients were only reviewed at the beginning and end of the 8 week	Unblinded own physician measurement (mercury sphyg) Control of BP (% ≤ 90mmHg DBP) Change in BP

										study period)	
Study	Setting and subjects	Mean Age (years)	Intervention subjects	Control Subjects	Length of follow up	Type & frequency of BP self measurement	Description of the control group	Intervention group regimen over and above control plus self-monitoring	Adjustment made for self-measurement readings	Was physician adjusting medication aware of self measurement readings?	Outcome measurement
Mehos 2000 US [34]	Primary care patients with treated hypertension and BP between 140-179/90-109mmHg	59	18	18	0 & 6 months	Manual electronic Daily Upper arm	Routine care with no restrictions on number of office visits.	Phone call from pharmacist	None specified	Yes	Clinic measurements before and after; not clear if blinded
Artinian 2001 US [35]	Family Community Centre. African-American men and women with BP≥ 140 and/or 90 (diabetic range ≥ 130/85)	59	6	9	0 & 3 months	Electronic, at home, minimum 3 times/week	Usual care; visits to primary care provider at intervals requested by the primary care provider.	Telemetry, patient education and nurse visit	None specified	Yes	Community centre pre and post by researcher who was blinded
Broege 2001 US [22]	Hypertension centre or community health centre. Hypertensive patients with BP< 150/90 if on treatment or >150/90 off treatment	73	20	20	0, 1, 2 & 3 months	Semi-automatic, 3 times morning and evening	Usual clinic treatment	Monthly clinic visit and nurse phone call	No adjustment	Yes	Clinic and Ambulatory SBP and DBP readings

Study	Setting and subjects	Mean Age (years)	Intervention subjects	Control Subjects	Length of follow up	Type & frequency of BP self measurement	Description of the control group	Intervention group regimen over and above control plus self-monitoring	Adjustment made for self-measurement readings	Was physician adjusting medication aware of self measurement readings?	Outcome measurement
Rudd 2004 US [36]	Primary Care clinics. Hypertensive patients with BP ≥ 140/90 or on anti-hypertensives, eligible for treatment under JNC VI criteria	59.5	74	76	0, 3, & 6 months	Automated, twice daily, at home	Routine care as received before study	Patient education and nurse phone call	Adjustment of 10/5mmHg	Yes	Blinded readings at 3 and 6 months. Drug monitoring using electronic pill count bottles
Baque # 2005 Spain [37]	Primary Care centres. Hypertensive patients with BP ≥ 140/90mmHg	61	622	703	0, 6, 8, 14, 16 & 24 wks	Automated, 15 days at weeks 6-8, and 14-16. 3 measurements in morning prior to medication, 2 in evening prior to supper.	None specified	No additional co-intervention	None specified	Encouraged to share with physician.	Control of BP (SBP <140mmHg, DBP <90mmHg)
Halme 2005 Finland [38]	Primary Health Care. Patients with essential hypertension, taking anyti-hypertensive treatment or BP ≥ 140/90	57	113	119	0 & 6 months	Automatic home readings. 1 week every 2 months, twice daily	Usual care; at regular local practice	No additional co-intervention	Adjustment of 5/5mmHg	Yes	Office BP taken with the home monitor. Change in SBP and DBP.

Study	Setting and subjects	Mean Age (years)	Intervention subjects	Control Subjects	Length of follow up	Type & frequency of BP self measurement	Description of the control group	Intervention group regimen over and above control plus self-monitoring	Adjustment made for self-measurement readings	Was physician adjusting medication aware of self measurement readings?	Outcome measurement
McManus 2005 UK [6]	Primary Care. Treated hypertensives with BP 140-200/85-100mmHg	62	214	227	0, 6, & 12 months	Electronic Upper Arm monthly in practice waiting room	Usual care	No additional co-intervention	No adjustment	Patients encouraged to share readings (approx 50% did)	Independently measured BP at 0,6 and 12 months
Zillich # 2005 US [39]	Community pharmacies. Treated hypertensives with BP 145-179/95-109 (diabetic = 135-179/90-109mmHg)	65	64	61	0, 4, & 12 wks	Automatic. 2 readings separated with 5 min rest, once daily in the morning	3 pharmacy visits over 3mths where BP measured nad referred to physician if >140/90mmHg	Patient education. Additional visit to implement treatment developed based on self readings.	No adjustment	Yes	Change in SBP and DBP
Marquez-Contreras 2006 Spain [19]	Primary care centres. Mild-moderate hypertension, requiring treatment (not all on treatment at BL)	59	100	100	0, 1, 3, & 6 months	Automatic. 3 days a week, twice before breakfast and twice before supper	Usual treatment from GP	No additional co-intervention	None specified	No, readings given to investigator who altered medications.	Mean decrease in SBP and DBP
Verberk 2007 Netherlands [13]	Setting, not clear. Office BP>139 and/or 89mmHg	55	214	216	0 & 12 months	Automated. 6 times a day for 7 days	Step-wise anti-hypertensive treatment based on office readings.	No additional co-intervention	No adjustment	Yes	Blinded. BP control and reduction

Study	Setting and subjects	Mean Age (years)	Intervention subjects	Control Subjects	Length of follow up	Type & frequency of BP self measurement	Description of the control group	Intervention group regimen over and above control plus self-monitoring	Adjustment made for self-measurement readings	Was physician adjusting medication aware of self measurement readings?	Outcome measurement
Green* a 2008 USA [14]	Medical Centres. Uncontrolled treatment hypertension	59	259	258	0 & 12 months	Automated. At least two days per week, twice per occasion	Usual care	Received hypertension pamphlet and patient web-site pamphlet Use of website plus patient education	Adjustment of 5/5mmHg	Yes	Blinded. BP control and changes in SBP and DBP
Green * b 2008 USA [14]	Medical centres. Uncontrolled treatment hypertension	59	261	258	0 & 12 months	Automated. At least two days per week, twice per occasion	Usual care	Received hypertension pamphlet and patient web-site pamphlet Use of website and pharmacist plus patient education	Adjustment of 5/5mmHg	Yes	Blinded. BP control and changes in SBP and DBP
Madsen 2008 Denmark [23]	General practices. Newlty diagnosed or treated but not controlled, office BP >150/95mmHg	56	113	123	0 & 6 months	Semi-automatic. 3x/wk in 1st 3 months, then once a wk during last 3 months. 3 readings each time.	Usual care	telemonitoring	Adjustment of 5/5mmHg	yes	Mean decrease in systolic and diastolic daytime ABPM.
Parati 2009 Italy [18]	Uncontrolled essential hypertension, BP ≥ 140/90, plus ABPM ≥ 130/80 with or without treatment	57.5	187	111	0, 4, 12 & 24 wks	Variable	Office based BP management	Nurse phone call and telemetry	Adjustment of 5/5mmHg	yes	Change in SBP and DBP

*study had three groups so included twice, once for each comparison Sphyg = sphygmomanometer # studies were cluster randomised by practice

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A Randomised Controlled Trial Of Telemonitoring And Self-Management In The Control Of Hypertension: Telemonitoring And Self-Management In Hypertension (TASMINH2)

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Summary

Background

Controlling blood pressure is a key aspect of cardiovascular disease prevention, but is currently suboptimal and until recently has been the sole preserve of health professionals. This study aimed to evaluate whether self-management by people with poorly controlled hypertension resulted in better blood pressure control.

Methods and Design

Patients were included if they were aged 35-85, had blood pressure >140/90mmHg despiteantihypertensive treatment and were willing to self-manage. They were randomised to self-management with telemonitoring and titration of antihypertensive medication or usual care. The primary end point was change in mean systolic blood pressure between baseline and each follow up point.

Findings

527 patients were recruited from 24 UK general practices and 91% had analysable data after one year. Systolic blood pressure was significantly lower in those that self-managed compared to usual care, by 3.7mmHg (95% CI 0.8, 6.6, p=0.013) reduction at six months and 5.4mmHg (95% CI 2.4, 8.5, p<0.001) after one year. Patients who self-managed increased their antihypertensive medication more than those receiving usual care but were no more anxious, had no more side effects and had slightly improved quality of life.

Interpretation

Self-monitoring with self-titration of antihypertensives and telemonitoring of blood pressuremeasurements is effective and feasible in UK Primary Care although only a minority may agree to such care. The blood pressure reduction achieved would be expected to lead to a 20% stroke risk reduction. Self-management should be offered to those with poorly controlled blood pressure.

Introduction

Raised blood pressure remains a key risk factor for cardiovascular disease, the largest cause of morbidity and mortality worldwide, yet only about a half of people on treatment for hypertension have their blood pressure controlled to current recommended levels.1, 2 This difficulty in achieving control is despite significant advances in the evidence base for both lifestyle and pharmaceutical interventions.3, 4 Therefore, there is a potentially important role for novel interventions to lower blood pressure, particularly in primary care, where the majority of management of hypertension takes place.

One such approach is patient self-management, which has gained widespread use in other chronic conditions such as diabetes 5 and anticoagulation control.6 Pre-requisites for self-management are the ability and willingness to self-monitor. A number of randomised controlled trials have demonstrated that self-monitoring of blood pressure can lead to blood pressure control that is at least as good as office monitored blood pressure, and may result in slightly better control, perhaps as a result of better adherence with therapy.7, 8 Self-management in hypertension has previously only been tested on a small scale (n=31) among individuals with chronic stable hypertension from primary and secondary care clinics9: a bespoke drug titration schedule incorporating current medications resulted in a lower daytime ambulatory mean arterial pressure of 2.9mmHg.

Another novel approach is telemonitoring, whereby readings made at home are relayed to a health care professional who can take appropriate action. This approach shows some promise in heart failure where it is associated with lower hospitalisation rates and reduced mortality.10 A systematic review in 2007 found 14 studies evaluating telemonitoring in hypertension of which only three were randomised controlled trials. These studies showed that home telemonitoring for hypertension can produce reliable and accurate data, and be well accepted by patients.11

The aim of the Telemonitoring and Self-Management of Hypertension Trial (TASMINH2) was therefore to evaluate whether self-management combining self-monitoring and self-titration with telemonitoring could lead to significant reductions of blood pressure sustained for a year.

Methods

Study design and participants

TASMINH2 was a prospective randomised open trial with automated ascertainment of end point. The detailed methodology has been reported elsewhere.12 Potential participants were identified by their own general practitioner using electronic searches of practice clinical record systems among 24 general practices in the West Midlands, United Kingdom (UK) between March 2007 and May 2008.13

Patients were eligible if they were aged 35-85, receiving treatment for hypertension with two or fewer antihypertensive drugs, had a blood pressure at baseline over 140/90 mmHg and were willing to self monitor and self-titrate medication. Exclusion criteria were blood pressure over 200/100 mmHg, postural hypotension (>20mmHg systolic drop), terminal disease, dementia, score of >10 on short orientation memory concentration test,14 hypertension not managed by their general practitioner or spouse already randomised to the study. Potentially eligible participants were invited by means of a letter and accompanying information sheet to attend a baseline clinic run at their practice by the research team.

Procedures

Eligibility was confirmed and consent obtained at the baseline clinic. Eligible patients were randomised to either intervention or control using a web based computerised system with telephone back up. Randomisation was stratified by general practice and minimised on sex, baseline systolic blood pressure (≤150 vs >150 mmHg) and presence or absence of diabetes or chronic kidney disease. All participants received information regarding non pharmacological interventions to reduce blood pressure based on literature produced by the British Hypertension Society.

Participants allocated to control received usual hypertension care. In the UK, national guidelines recommend (and performance related pay rewards) an annual review to monitor blood pressure, provide support and discuss lifestyle, symptoms and medication.15, 16 Following randomisation, all control participants were asked to attend for a review by their general practitioner. No specific instructions were given to the content of this other than medication should be reviewed and thereafter care was at the discretion of the general practitioner.

Patients randomised to the intervention were invited to two training sessions run by the research team. Participants were trained to monitor their own blood pressure for the first week of each month using a validated automated sphygmomanometer (Omron 705IT) and to transmit blood pressure readings to the research team using an automated modem device (i-modem, Netmedical, NL).17 A colour "traffic light" system was used by participants to code readings as green (below target but above safety limit), amber (above target but below safety limits) and red (outside of safety limits) [see web appendix for coding chart]. Titration schedules comprising two changes or increases in medication were agreed between

participants and their general practitioner at a review following training and included the option for renal monitoring for ACE inhibitors. The general practitioner received no specific instruction from the research team as to what medication changes to make other than being given a copy of the current NICE guidelines.16 Patients were instructed to make medication changes following the titration schedule if they had two consecutive months of readings above target by requesting a new prescription without needing to be seen by their general practitioner. Monthly summaries of each participant's blood pressure were sent to their general practitioner.

Target blood pressures for home based measurements were based on the then current UK NICE guidelines for hypertension and diabetes, adjusted down by 10/5 mmHg in accordance with the recommendations of the British Hypertension Society resulting in home targets of 130/85 mmHg and 130/75 mmHg respectively.16, 18, 19 In the absence of National recommendations for self-monitoring of blood pressure in chronic kidney disease (CKD), patients with CKD were assigned the same target as those with diabetes. Safety limits of readings greater than 200/100 mmHg or less than 100 mmHg systolic triggered the patients to request a blood pressure check by the practice and a "Freephone" telephone number was provided for any trial related queries. Research team intervention on the basis of telemonitored blood pressure results was limited to checking that participants had followed the safety advice for high or low readings by means of a telephone call.

The primary outcome for the study was change in systolic blood pressure between baseline and six and twelve months. Follow-up was performed by members of the research team in the patient's general practice. At both baseline and follow up visits, blood pressure was measured systematically following five minutes rest using a validated electronic automated sphygmomanometer (BP-TRU BPM 100 or 200, BC, Canada).20 Six blood pressure readings were taken at one minute intervals. The

mean of the second and third readings was used in the primary outcome. Outcome measurement was not blinded but utilised the automatic mode of the sphygmomanometer to measure the blood pressure without the need for researcher intervention other than to place the cuff and switch on.

Medications prescribed were recorded from the electronic patient record with confirmation from the patient and side effects and anxiety were measured using standard uestionnaires.21, 22

Statistical Analysis

A sample size of 239 people per group was required to detect a blood pressure difference of at least 5 mmHg between groups with 90% power, assuming a standard deviation of 15 mmHg, and 20% drop out.23 The study was powered on the primary analysis alone. The primary analysis took an intention to treat without imputation approach. A mixed model methodology was used to compare intervention and control patients in their within subject variation in systolic blood pressure between baseline and six and twelve months. The primary analysis was adjusted for practice (as a random effect), and covariates baseline blood pressure, gender and diabetic / CKD status. The impact of any significant differences was further investigated by examining the individual changes in systolic blood pressure between baseline and the follow up points at six and twelve months. Normally distributed errors were assumed and residuals were checked for normality using the Kolmogorov Smirnov test. Predefined sub groups for the primary analysis were based on blood pressure target, age (65 as threshold), gender, baseline systolic blood pressure (150 mmHg threshold) and deprivation [the latter was added to the analysis plan prior to analysis]. Secondary analyses used similar techniques to investigate change in diastolic blood pressure, side effects and anxiety. For number of medications and use of specific medications, generalised linear models were used when adjusting for the covariates mentioned previously. Unadjusted tests and confidence intervals were computed assuming Poisson and Binomial distributions respectively.

This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN17585681.

Role of the funding source

This study received joint funding from the UK Department of Health Policy Research Programme, National Coordinating Centre for Research Capacity Development and Midlands Research Practices Consortium (MidReC). Service support costs were obtained from the Department of Health in

collaboration with MidReC. None of the funders had a direct role in study design, in data collection, analysis or interpretation, in writing the report, or in the decision to submit for publication.

Results

7637 potentially eligible individuals were invited to participate of whom 1650 attended a randomisation clinic. 1123 were not eligible of which by far the commonest reason (916, 82%) was that blood pressure measured by the research nurses was below the inclusion criteria (140/90 mmHg). In total 527 people were randomised from 24 practices (range per practice 8-56) of whom 480 (91%) attended both 6 month and 12 month follow up and had complete data for the primary outcome (complete cases). Two patients attended follow up but had no blood pressure data due to intolerance of measurement in one case and a machine error in the other. Figure 1 shows the flow through the trial and Table 1 shows the baseline details of the complete cases which were similar in both groups.

A median of 152 blood pressure readings were taken by each patient in the intervention group. 60 (23%) patients recorded at least one blood pressure reading outside of the study limits (>200/100 mmHg or <100/mmHg) and 9 (3%) were telephoned by the research team in response to such high/low telemonitored readings where the patient had not contacted the research team and it was not clear that the blood pressure had settled on repeated measurement.

Overall, blood pressure changed significantly in the intervention group compared to the control group (p=0.002) (table 2). Blood pressure reduction from baseline in the intervention group was greater compared to the control group by 3.7 mmHg (95% CI 0.8 to 6.6, p=0.013) at six months and 5.4 mmHg (95% CI 2.4 to 8.5, p<0.001) at twelve months.

No difference was seen in change in blood pressure between sub groups (see figure 2) with the exception of social deprivation: a greater reduction in systolic blood pressure was seen in the less deprived (5.3 mmHg (1.9, 8.8) at 6 months; 7.0 mmHg (3.5, 10.6) at 12 months) compared to the more deprived (-0.4 mmHg (-5.9, 5.2) at 6 months; 1.6 mmHg (-4.4, 7.6) at 12 months) (p=0.05 and 0.08 respectively for the comparison of change at 6 and 12 months between the two groups).

The primary analysis was repeated using the mean of readings 2-6 rather than 2 and 3 to assess the influence of habituation to blood pressure measurement on results, and whilst baseline blood pressure was lower, the effect size in terms of the additional blood pressure drop in the intervention group was similar to that in the primary analysis (3.4mmHg (0.7, 6.2) at six months and 5.2 mmHg (2.3, 8.0) at 12 months).

The pattern of the trend over time for the mean of diastolic blood pressure (readings 2 and 3) was not significantly different between the intervention group and the control group (p=0.092). The mixed model analysis did not show a significant difference in the magnitude of change between the intervention and control groups in DBP from baseline to 6 months (1.3mmHg, 95% CI = -0.3 to 2.6, p = 0.108) but did between baseline to 12 months (2.7mmHg 95% CI 1.1 to 4.2, p=0.001).

Of the 210 (80%) patients who self-managed for the full 12 months of the study, 148 (70%) made at least one medication change (median 1, IQR 0, 2). From baseline to six months there were 0.32 (0.21, 0.43) additional antihypertensives in the intervention group (p =0.001) and baseline to 12 months 0.46 (0.34, 0.58) additional antihypertensives, (p =0.001). There was a greater increase in the intervention group over the year for both thiazides (36.8% to 53.0% (intervention group) vs 37.0% to 43.5% (control), p<0.05) and calcium antagonists (30.8% to 50.4% (intervention group) vs 29.3% to 32.7% (control group), p<0.001) (table 3).

Intervention patients attended 3.2 (2.9, 3.5) primary care consultations which included blood pressure measurement and/or management through the year compared to 3.5 (3.2, 3.7) in the control group (c2 (1) =3.0, p=0.08 for the comparison).

Only the side effect of leg swelling was more common in the intervention group (see table 4). There was no significant difference in state anxiety score at baseline nor over time (change 0-12m 0.6 (0.1, 1.1) vs 0.65 (0.1, 1.1)) [intervention vs control respectively]. Quality of life as measured by the EQ5D had a trend towards increasing in the intervention group compared to the control group but was not significantly different (table 5).

After 12 months of the study, patients in the intervention group were more likely than patients in the control group to rank self-monitoring as their preferred method of blood pressure monitoring (166/234 = 70.9% v 103/242 = 42.6%) ($p<0.001$).

Discussion

This is the first study to show that taking regular BP self-measurements and following a simple predetermined antihypertensive titration plan is more effective in lowering systolic BP than usual care over the period of a year. The absolute reduction in blood pressure (5.4/2.7 mmHg) is equivalent to a reduction in stroke risk of over 20% and CHD risk of over 10%.3 Sub group analyses were not powered *a priori* and there were no clear subgroup differences except that the less deprived achieved lower blood pressures.

The greater blood pressure reduction in the self-management group was probably mediated via increased medication, particularly calcium antagonist and thiazide classes, and reflecting the NICE guidelines.16 Alternative explanations could include the different targets used and the effect of selfmonitoring per se or the additional effect of telemonitoring. However, the effects were greater than those reported in systematic reviews which have not differentiated between the effect of self-monitoring and that of any associated co-intervention.7 The home target chosen was recommended by the British Hypertension Society - but lower than the European Hypertension Society and American consensus conference recommendations published after the trial had recruited The evidence for setting such therapeutic targets is not yet clear but targets used in the current study were in line with contemporary norms.24

Telemonitoring was used to check that participants had adhered to safety advice. However, few patients required telephone reminders to take action for high or low readings. Participating practices received summaries of month mean blood pressures but the onus was on self-management unlike other trials which have used technology to prompt physician or nurse intervention.10, 11 The increasing capacity for integrating home measured blood pressures into the electronic patient record (personal communication George Mac Ginnis, Programme Manager, Assistive Technology, NHS Technology Office) might drive increased use of telemonitoring.

Change in diastolic blood pressure did not differ significantly overall although the change between baseline and final follow up was significant. This may be an issue of lack of power. Blood pressure in the control group dropped by 12.2/4.8 mmHg which could have masked the true effect size of the intervention, and was probably due to both regression to the mean and an increase in medication, particularly thiazides. Intervention increased neither anxiety nor overall side effects - with the exception of leg swelling which was probably due to increased calcium antagonist use. Quality of life was no worse in the intervention group compared to the controls despite increased medication. Taken together these data suggest that self-management does not appear to lead to important adverse effects or reduced quality of life.

After 12 months, 80% continued to self-manage which compares favourably with drug treatment in hypertension where 29% have stopped a new medication after 12 months.25 Patients who self-managed rated selfmonitoring most highly at the end of the trial.

The study was not blinded but the primary end point was measured using automated sphygmomanometers allowing consecutive BP readings to be taken without requiring intervention from the researcher once the cuff is in place and the machine turned on. The sensitivity analysis using the mean of multiple blood pressure measurements to reduce the impact of the alerting response to blood pressure measurement gave very similar results to the primary analysis albeit at lower absolute blood pressure which suggests that habituation to blood pressure measurement in the intervention group did not influence the results.

Generalisability is a key issue in all research. This trial was conducted within primary care, the principal setting for hypertension management but only recruited a minority of potentially eligible individuals as has been seen in other studies of self-management.26 Participants were less deprived than average and ethnic minorities under represented. Taken together then, despite the success of the intervention, selfmanagement will not be suitable for all, but if only 20% of hypertensives self-managed, this would still represent around 4% of the UK population i.e. more than two million individuals.

The only other previous study investigating self-management of hypertension was a Canadian study which used a fixed titration regime, had short follow up (8 weeks) and only randomised 31 patients. Although the primary outcomes are not directly comparable (ABPM v office BP), both studies have

reported a greater decrease of blood pressure in the self-managing patients.9 In related work, selfmonitoring of blood glucose has been found to be effective for patients with diabetes where insulin is prescribed. 5 A systematic review found that optimal self-management of asthma medication may be achieved by either self-adjustment following a written action plan or by regular medical review.27 A further review showed that self-testing of INR and self-adjusting of warfarin results in at least as good control of anticoagulation compared to usual care by GPs or a specialist service.6

In conclusion, self-management of hypertension resulted in significant and worthwhile reductions in blood pressure which were maintained at both six and twelve months. The reduction in blood pressure appeared to be mainly due to the increase in the number of anti-hypertensive drugs prescribed by following a simple titration plan compared to usual care. Importantly, anxiety levels and side effects were not affected by practicing self-management of hypertension. Self-management of hypertension represents an important new addition to the management of hypertension in primary care.

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Ethical approval

The study received a favourable ethical opinion by Sandwell and West Birmingham Local Research Ethics Committee reference 05/Q2709/103.

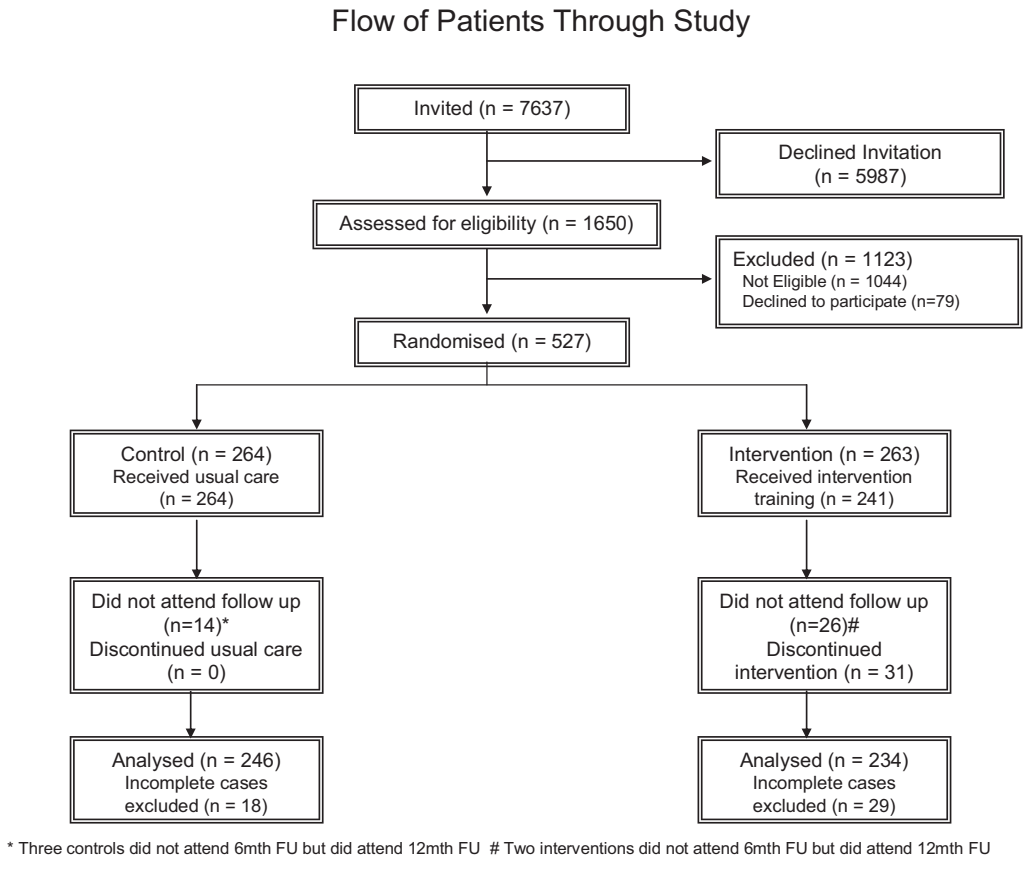
Author contributions

RJM led the study and wrote the first draft of the manuscript. RH and BK undertook the analyses. All authors participated in the design, execution and oversight of the study. All authors had access to the data, commented on subsequent drafts and have approved the final submitted version. RJM will act as guarantor and made the final decision to submit for publication.

Conflict of Interest Statement

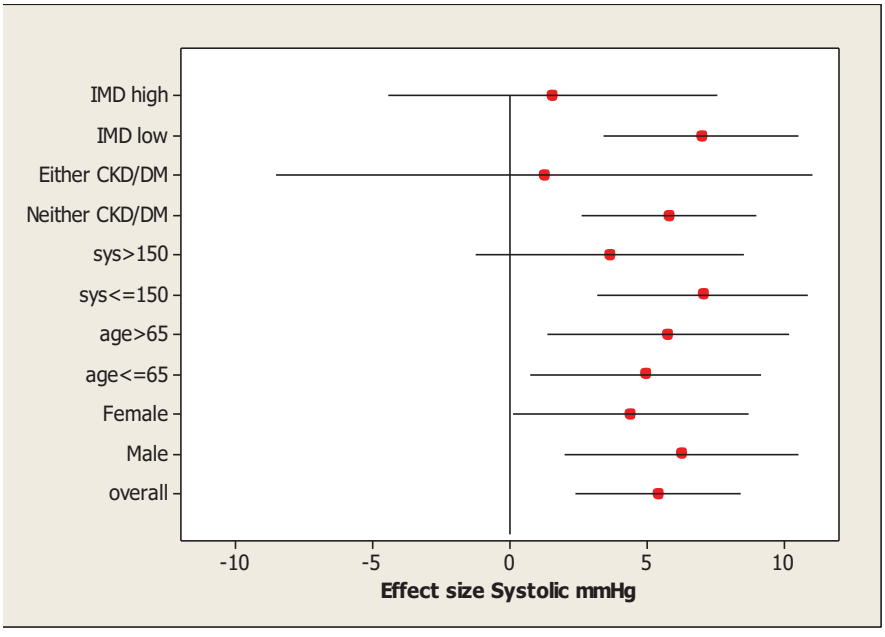
RJM is funded by an NIHR Career Development Fellowship. He received a consultancy fee from Tplus Medical (2006) to advise on telemonitoring services. FDRH has received limited research support in terms of BP devices from Microlife and BpTRU and occasional sponsorship or speaker fees from a number of pharmaceutical companies that market anti-hypertensives. All other authors have no conflicts to declare.

Figure 1: Trial Profile



* Three controls did not attend 6mth FU but did attend 12mth FU # Two interventions did not attend 6mth FU but did attend 12mth FU

Figure 2: Effect size by sub group for systolic BP over 12 months



Sub group comparison p values	
IMD	p=0.08
CKD/DM p=0.29	p=0.29
Sys	p=0.19
Age	p=0.67
Gender	p = 0.66

Effect size = intervention (Baseline-12 months readings) – control (Baseline -12 months readings)
(reading = mean of second and third systolic BP mmHg)
IMD = Index of Multiple Deprivation; CKD = Chronic Kidney Disease; DM = Diabetes
sys = Baseline systolic blood pressure.

Table 1: Baseline characteristics of 480 complete cases (unadjusted)

Attribute		Intervention * n= 234	Control * n = 246
Mean Age (years)		66.6 [8.8]	66.2 [8.8]
Male sex n (%)		110 (47.0%)	115 (46.7%)
Mean Systolic Blood Pressure (mmHg)		152.1 [11.9]	151.8 [11.9]
Mean Diastolic Blood Pressure (mmHg)		85.0 [8.5]	84.5 [9.6]
Ethnic Group n (%) =	White	223 (95.3%)	238 (96.7%)
	Black	5 (2.1%)	2 (0.8%)
	Asian	4 (1.7%)	6 (2.4%)
	Other	2 (0.9%)	0
Mean Body Mass Index (kg/m^2)		29.6 [5.8]	30.0 [5.4]
Marital Status = married, n (%)		174 (74.4%)	188 (76.4%)
Occupation n (%) =	Professional/managerial and technical	110 (47.0%)	109 (44.3%)
	Skilled manual and non manual	73 (31.2%)	90 (36.6%)
	Partly skilled and unskilled	13 (5.6%)	17 (6.9%)
	Unemployed/unwaged	38 (16.2%)	30 (12.2%)
Mean Index of Multiple Deprivation		16.7 [13.3]	17.3[14.0]
Smoking status = current smoker n (%)		19 (8.1%)	14 (5.7%)
Mean Anxiety score (STAI 6 (range 6-24))		10.1 [3.3] (n*=4)	9.7 [3.1] (n*=6)
PMH Coronary Heart Disease n (%)		22 (9.4%)	24 (9.8%)
PMH Cerebrovascular Disease n (%)		12(5.1%)	9 (3.7%)
PMH Diabetes n (%)		18 (7.7%)	17 (6.9%)
PMH Chronic Kidney Disease n (%)		17 (7.3%)	27 (11.0%)
PMH Atrial Fibrillation		19 (8.1%)	18 (7.3%)
Mean number of anti hypertensive drugs		1.50 [0.53]	1.54 [0.51]

*figures in square brackets [] = standard deviation

**= Mann Whitney test (otherwise t test)

n= number, n*=number missing, STAI = State trait anxiety inventory, PMH = Past medical history

Table 2: Systolic and diastolic blood pressure values

	Mean Blood Pressure			Mean differences		Effect sizes	
	Baseline	**Six months**	**12 months**	**0-6 months**	**0-12 months**	**0-6 months**	**0-12 months**
Mean Systolic Blood Pressure (mmHg) [unadjusted]							
Intervention	152.1 [150.6, 153.6]	139.0 [137.0, 141.0]	134.9 [132.6, 137.1]	13.1 [10.9, 15.3]	17.2 [14.8, 19.7]	3.7 mmHg [0.6, 6.8]	5.5 mmHg [2.2, 8.8]
Control	151.8 [150.3, 153.3]	142.4 [140.2, 144.6]	140.1 [138.0, 142.2]	9.4 [7.2, 11.6]	11.7 [9.5, 13.9]		
Mean Systolic Blood Pressure (mmHg) [adjusted for practice, baseline blood pressure >150, diabetic/CKD status and sex]							
Intervention	151.9 [150.8, 153.1]	138.8 [136.6, 141.0]	134.7 132.3, 137.0]	12.9 [10.4, 15.5]	17.6 [14.9, 20.3]	3.7 mmHg [0.8, 6.6]	5.4 mmHg [2.4, 8.5]
Control	152.0 [150.9, 153.2]	142.6 [140.5, 144.8]	140.3 [138.0, 142.6]	9.2 [6.7, 11.8]	12.2 [9.5, 14.9]		
Mean Diastolic Blood Pressure (mmHg) [unadjusted]							
Intervention	85.0 [83.9, 86.1]	79.6 [78.4, 80.9]	77.4 [76.1, 78.6]	5.4 [4.3, 6.5]	7.6 [6.5, 8.8]	1.3 mmHg [-0.3, 2.8]	2.7 mmHg [1.1, 4.3]
Control	84.5 [83.3, 85.7]	80.3 [79.0, 81.7]	79.5 78.1, 80.9]	4.1 [3.0, 5.3]	5.0 [3.8, 6.1]		
Mean Diastolic Blood Pressure (mmHg) [adjusted for practice, baseline blood pressure >150, diabetic/CKD status and sex]							
Intervention	85.2 [83.8, 86.5]	79.8 [78.3, 81.3]	77.5 [76.0, 79.1]	5.2 [3.9, 6.5]	7.5 [6.0, 9.0]	1.3mmHg, [-0.3, 2.6]	2.7mmHg [1.1, 4.2]
Control	84.7 [83.4, 86.0]	80.6 [79.1, 82.0]	79.8 [78.3, 81.3]	3.9 [2.7, 5.2]	4.8 [3.4, 6.3]		

Mean differences from baseline.

All figures are mean (95% confidence intervals)

Table 3: Overall number of antihypertensive medications and by main classes

					Significance testing		
Medication		**Baseline**	**6 months**	**12 months**	**Overall Trend comparison[1]**	**0 – 6m comparison[2]**	**0 – 12m comparison[2]**
Mean number of Antihypertensive drugs$	Intervention Control	1.5 (1.3-1.7) 1.5(1.4-1.7)	1.9 (1.8-2.1) 1.7 (1.5-1.8)	2.1 (1.9-2.3) 1.7 (1.5-1.8)	p<0.001	p<0.001	p<0.001
Thiazide#	Intervention Control	86 (36.8%) 91 (37.0%)	118 (50.4%) 107 (43.7%) n*=1	124 (53.0%) 107 (43.5%)	p<0.05	p<0.05	p<0.05
Beta blocker#	Intervention Control	41 (17.5%) 45 (18.3%)	44 (19.0%) n*=2 36 (14.8%) n*=2	42 (17.9%) 40 (16.2%)	p<0.05	p<0.05	ns
ACE#	Intervention Control	95 (40.6%) 108 (43.9%)	113 (48.7%) n*=2 114 (46.5%) n*=1	113 (48.3%) 117 (47.6%)	ns	ns	ns
ARB#	Intervention Control	46 (19.7%) 41 (16.7%)	60 (25.8%) n*=1 48 (19.7%) n*=2	67 (28.6%) 48 (19.5%)	ns	ns	p<0.05
CAB#	Intervention Control	72 (30.8%) 72(29.3%)	105 (45.3%) n*=2 80(32.7%) n*=1	118 (50.4%) 76 (30.9%)	p<0.001	p<0.001	p<0.001

[1] Comparison of trend over time between intervention and control adjusted for practice baseline blood pressure >150, diabetic/CKD status and sex.

[2] Comparison of change from baseline to 6 or 12 months between intervention and control also adjusted as above.

CAB: Calcium Channel Blocker, ACE Angiotensin Converting Enzyme Inhibitors, ARB: Angiotensinogen Receptor Blocker

$ number (95% confidence interval) # n (%) prescribed at each time point n* = missing data

Table 4: Top ten symptoms / side effects by randomisation group at 12 months

Side effect / symptom	Intervention	Control	P value
Stiff joints	95 (41%)	104 (42%)	0.71
Pain	89 (38%)	84 (34%)	0.37
Fatigue	84 (36%)	78 (32%)	0.33
Swelling of legs	74 (32%)	55 (22%)	0.02
Sleep Difficulties	72 (31%)	80 (33%)	0.68
Dry mouth	68 (29%)	59 (24%)	0.21
Feeling flushed	61 (26%)	57 (23%)	0.46
Cough	61 (26%)	60 (24%)	0.67
Breathlessness	53 (23%)	59 (24%)	0.73
Sore eyes	48 (21%)	58 (24%)	0.42

Table 5: Quality of Life as measured by EQ5D

	Values			Adjusted mean differences		Effect sizes	
	Baseline	**Six months**	**12 months**	**0-6 months**	**0-12 months**	**0-6 months**	**0-12 months**
EQ5D [Unadjusted]							
Intervention	0.809 [0.781, 0.837]	0.819 [0.789, 0.850]	0.833 [0.805, 0.861]	0.010 [-0.013, 0.032]	0.024 [0.002, 0.047]	0.010 [-0.024, 0.043]	0.028 [-0.011, 0.060]
Control	0.847 [0.819, 0.876]	0.848 [0.818, 0.877]	0.844 [0.814, 0.873]	0.000 [-0.028, 0.026]	-0.004 [-0.030, 0.020]		
EQ5D [adjusted for practice, baseline blood pressure >150, diabetic/CKD status and sex]							
Intervention	0.801 [0.767, 0.834]	0.812 [0.777, 0.847]	0.826 [0.792, 0.859]	0.011 [-0.013, 0.034]	0.024 [-0.001, 0.049]	0.011 [-0.023, 0.045]	0.027 [-0.004, 0.065]
Control	0.841 [0.809, 0.874]	0.842 [0.807, 0.876]	0.838 [0.805, 0.871]	0.000 [-0.023, 0.023]	-0.003 [-0.027, 0.021]		

Mean [Bootstrapped 95% Confidence Intervals]

The Colour Coding Chart

In each case the top reading is the SYS and bottom reading DIA

Colour	Level	Blood Pressure	Action
RED	HIGH	**SYS 201 or more OR DIA 101 or more**	Your BP is too high. Make an appointment within 48 hours to see your GP or nurse. Record a RED reading
AMBER	RAISED may need to alter medication	**SYS 131-200 OR DIA 86-100**	Your BP is raised. Record an AMBER reading If FOUR or more AMBER readings in one week on **2 consecutive months** then look at your medication change instructions.
GREEN	NORMAL	**SYS 101-130 AND DIA 85 or less**	Your BP is normal. This is fine provided that you have no side effects. Record a GREEN reading
RED	LOW	**SYS 100 or less**	Your blood pressure is too low Make appointment to see your GP Record a RED reading

Don't forget to keep up your healthy diet, exercise and sensible drinking as set out in the self-help information

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