## **ORIGINAL ARTICLE**

# The Effect of Self-Monitoring of Blood Pressure on Medication Adherence and Lifestyle Factors: A Systematic Review and Meta-Analysis

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#### BACKGROUND

Self-monitoring of blood pressure (SMBP) can contribute to reduced blood pressure in people with hypertension. Potential mediators include increased medication, improved adherence, and changes in lifestyle factors including dietary change and increased physical activity. The objective of this review was to determine the effect of SMBP on medication adherence, medication persistence, and lifestyle factors in people with hypertension.

#### METHODS

Electronic bibliographic databases were searched through February 2014 to identify randomized controlled trials that compared SMBP to control/usual care in ambulatory hypertensive patients and reported medication or nonpharmacologic treatment adherence measures.

#### RESULTS

Twenty-eight trials with 7,021 participants fulfilled the inclusion criteria. Medication adherence was assessed in 25 trials (89%), dietary outcomes in 8 (29%), physical activity in 6 (21%), and medication persistence in 1 (4%). Blood pressure was assessed in 26 studies (93%). Follow-up ranged from 2 weeks to 12 months. Pooled results of 13 studies demonstrated a small but significant overall effect on medication adherence in favor of SMBP interventions (standardized mean difference 0.21, 95% CI

Self-monitoring of blood pressure (SMBP) leads to reduced blood pressure (BP) in people with hypertension, but how this change occurs is not well understood.<sup>1-3</sup> Potential explanations include pharmacological (increased medication, better adherence) or nonpharmacological (diet, alcohol, exercise, weight loss) mediators. Understanding which mediating factors are important could allow optimization of future interventions.

Around 25% of patients initiated on hypertensive medication fail to fill their first prescription.<sup>4</sup> In the first year of antihypertensive treatment, patients on average have possession of medication for 50% of the time, and only 20% have sufficiently high adherence to achieve any benefit.<sup>5</sup> Improving adherence is therefore a key target for behavioral interventions. Lifestyle change is another target as it has been estimated that diet and weight loss can be at least as effective as single drug therapy at reducing BP.<sup>6</sup>

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Initially submitted December 5, 2014; date of first revision December 22, 2014; accepted for publication January 16, 2015; online publication February 26, 2015.

0.08, 0.34), with moderate heterogeneity ( $l^2 = 43\%$ ). Standardized mean difference was used to express the size of intervention effect in each study relative to the variability observed, and was used to combine the results of studies where different measures of medication adherence were used. Where SMBP interventions had a significant effect on lifestyle factor change, the effect was unlikely to be clinically significant. Pooled results of 11 studies demonstrate a significant overall effect on diastolic blood pressure in favor of SMBP (weighted mean difference –2.02, 95% Cl –2.93, –1.11), with low heterogeneity ( $l^2 = 0\%$ ). A test for subgroup differences showed no difference was significantly improved or not.

#### CONCLUSIONS

SMBP may contribute to improvements in medication adherence in hypertensives. However, evidence for the effect of SMBP on lifestyle change and medication persistence is scarce, of poor quality, and suggests little clinically relevant benefit.

*Keywords:* adherence; blood pressure; hypertension; meta-analysis; non-pharmacologic; self-monitoring.

doi:10.1093/ajh/hpv008

A systematic review published in 2006 found that 6 of 11 included trials detected a statistically significant improvement in adherence to antihypertensive medication from SMBP.<sup>7</sup> Limited evidence from qualitative research suggests that SMBP can influence compliance with diet and exercise regimes.<sup>8,9</sup>

The primary objectives of this review were to synthesize the literature to determine the effect of SMBP on medication adherence, medication persistence, and lifestyle factors in people with hypertension.

#### METHODS

#### Information sources and study selection

Electronic databases (DARE, Cochrane Database of Systematic Reviews, MEDLINE, EMBASE, CINAHL,

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© American Journal of Hypertension, Ltd 2015. All rights reserved. For Permissions, please email: journals.permissions@oup.com PsycINFO, Proquest Dissertation, and Theses) were searched from inception to February 2014 to identify randomized trials of interventions including SMBP compared with control groups without SMBP. Ongoing and completed studies without related publication were identified through searches of clinical trial databases (i.e., ClinicalTrials.gov, WHO trials portal, UKHTA, and Current controlled trials).

The search strategy was developed in Medline and translated for use in the other databases (Supplementary Appendix S1). No language or time restrictions were applied. Studies were also identified through citation searches of related reviews and relevant trials, and authors were contacted for further information wherever necessary.<sup>10</sup>

Randomized and quasi-randomized trials were eligible for inclusion if the participants had hypertension, were receiving care in ambulatory/outpatient settings, and if medication adherence and/or lifestyle factor outcomes were available. Two reviewers independently screened the reports for inclusion (B.F., J.H.B.). A protocol was developed and made available on the PROSPERO database prior to commencing the review.<sup>11</sup>

#### Data extraction and risk of bias assessment

Data were extracted on setting, demographics, intervention and control characteristics, and outcome measures. Raw unadjusted data were extracted wherever available.

Primary outcomes of interest were antihypertensive medication adherence and persistence, dietary outcomes, alcohol consumption, and physical activity. Medication adherence measures were divided into 4 groups to aid analysis: electronic monitoring, pill counts, pharmacy fill data, and self-reported measures. Secondary outcomes included BP, BP control, and adherence to the SMBP component of interventions.

Studies were classified according to whom the intervention was aimed at (patients and/or healthcare professionals (HCPs)), and any cointerventions beyond SMBP.

Data extraction and risk of bias assessment were carried out independently by 2 reviewers (B.F., J.H.B.). Following guidance from the Cochrane Collaboration, studies were deemed to be at high, low, or unclear risk of bias based the following factors: random sequence generation, allocation concealment, blinding of outcome assessment, selective reporting, and attrition.<sup>12</sup> Risk of bias across studies was assessed using a Funnel plot and Egger's test.

#### **Statistical analysis**

Meta-analyses were performed with RevMan 5 using random-effect models for a comparison of SMBP vs. usual care/ control for medication adherence and BP outcomes. Metaanalysis was not undertaken for lifestyle factor outcomes due to insufficient data. As medication adherence was measured in different ways, standardized mean differences (SMD) were calculated in order to compare adherence across studies. Subgroup analyses were used to group studies that measured medication adherence by type of measurement. Where studies reported a number of adherence measures, the most objective measure was used. Meta-regression explored the association between BP change and medication adherence. The *I*<sup>2</sup> statistic was used to present statistical heterogeneity for all meta-analyses.

#### RESULTS

#### **Included studies**

Twenty-eight trials with a total of 7,021 participants fulfilled the inclusion criteria (Figure 1).<sup>13–40</sup> Medication adherence was assessed in 25 trials (89%) dietary outcomes in 8 (29%), physical activity in 6 (21%), and medication persistence in 1 (4%). BP was also assessed in 26 (93%) studies.

Characteristics of included studies are summarized in Table 1. SMBP was the sole component of interventions in 11 studies (39%) and combined with cointerventions in 17 (61%). Cointerventions were coded and grouped using *a priori* categories and are summarized in Table 1, and in more detail in the Supplementary Appendix S2. The most common cointervention was education delivered either verbally (in 11 studies) or using either printed or online materials (in 6 studies).

SMBP interventions may target behavior change in patients (i.e., improving treatment adherence, self-titration of medication, etc.). Equally, SMBP interventions can target behavior change in HCPs (i.e., medication prescribing, overcoming clinical inertia). Patients alone were the target of the intervention in 8 studies, while interventions targeted both patients and HCPs in the remaining 20. In the majority of cases where both patients and clinicians were targeted, intervention participants' general practitioners (GPs, family physicians) received self-measured BP results from participants, or were informed when patients exceeded target BP, and were able to act accordingly.<sup>13,14,18,22,27-31,34,37,40</sup> Three studies involved pharmacists implementing the intervention, 2 involved nurses, and 1 involved dieticians. The theoretical basis for the development of the intervention was reported in only 4 studies.<sup>19,30,33,35</sup>

Participants were initiated on new antihypertensive medications in 4 studies,<sup>16,25,37,38</sup> and medication titration protocols based on self-measured BP were reported in 5.<sup>16,24,35,37,40</sup>

Protocols for self-monitoring varied across studies, ranging from participants being asked to measure their BP twice daily every day,<sup>23</sup> to monthly.<sup>27</sup> The SMBP protocol was not reported in 5 studies.<sup>14,16,26,32,36</sup>

Follow-up ranged from 2 weeks to 12 months with a median of 6 months, and was deemed to be adequate (i.e., >80% of participants available for outcome assessment at follow-up) in 75% of studies.

#### **Risk of bias**

Two studies were judged to be at low risk of bias;<sup>24,35</sup> 12 studies were judged to be at high risk of bias in at least

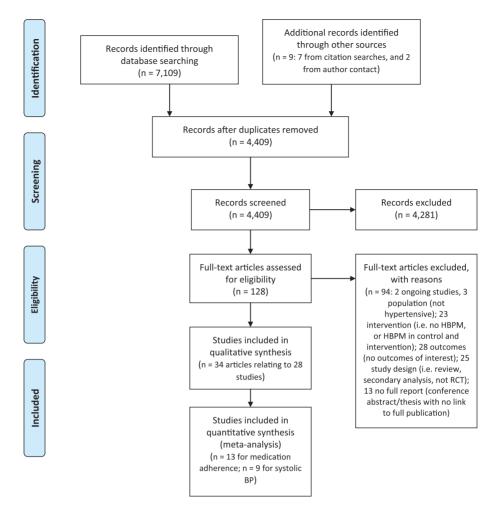


Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.

1 domain.<sup>14,17,21,22,27,29-31,33,34,36,38</sup> Results were unclear for the remaining 14 studies, most commonly due to lack of detail regarding allocation concealment. Risk of bias for each domain in each included study is presented in Figure 2.

#### Adherence and persistence to antihypertensive medication

Adherence to antihypertensive medication was assessed by electronic monitoring in 5 studies, by pill count in 8, using pharmacy fill data in 6, and by self-report in 9. Three trials used 2 categories of measure.<sup>23,36,37</sup> Full results of medication adherence are presented in Table 2.

Pooled analysis of all adherence measures demonstrated a small but significant overall effect in favor of SMBP (SMD 0.21, 95% CI 0.08, 0.34; 13 studies), with moderate heterogeneity ( $I^2 = 43\%$ ) (Figure 3). A test for subgroup differences did not suggest a significant association between adherence measures and overall effect size ( $\chi 2 = 5.47$ , df = 3, P = 0.14). We carried out a sensitivity analysis removing self-reported measures from the meta-analysis, and this had a small impact on the overall effect: SMD 0.27 (95% CI 0.11–0.34), compared to 0.21 (95% CI 0.08–0.44); with a small increase in heterogeneity:  $I^2$  46% compared to 43%. When assessed by electronic monitoring (i.e., medication event monitoring systems), the pooled result of 2 studies detected a significant effect in favor of the intervention (SMD 0.45, 95% CI 0.10–0.79), with moderate statistical heterogeneity ( $I^2 = 59\%$ ). The pooled result of 5 studies where adherence was assessed by pill counts showed a small significant effect size in favor of the intervention (SMD 0.30, 95% CI 0.01–0.59), with moderate statistical heterogeneity ( $I^2 = 42\%$ ).

Assessment of adherence using pharmacy fill data (2 studies) and self-report (4 studies) showed no significant effect in favor of the intervention (SMD 0.12, 95% CI –0.05 to 0.29 and SMD 0.05, 95% CI –0.13 to 0.22, respectively), with low statistical heterogeneity in both cases ( $I^2 = 0\%$ ). Medication persistence was assessed in 1 study.<sup>16</sup> No significant effect in favor of SMBP was found in the proportions not discontinuing their medication by the end of the trial (9 months).

Rates of adherence in the included randomized controlled trials tended to be high, e.g., >97%,<sup>21</sup> >93%,<sup>26</sup> 90%,<sup>37</sup> and >88%<sup>13</sup>.

#### Lifestyle factors: diet and physical activity

Diet and physical activity outcomes are presented in Table 3.

	Number of							
Study id, Country	participants	s Study arms included in review	Follow-up	SMBP protocol	Target <sup>a</sup>	Age	% Female	e Outcomes <sup>b</sup>
Bailey, <sup>13</sup> Australia	62	(i) SMBP (ii) Usual care	8 weeks (2 months)	Sitting twice daily (AM and PM)	P + HCP	55	54	MA, BP, AI
Bove, <sup>14</sup> USA	241	<ul> <li>(i) SMBP, telemedicine, and education (print/ online materials)</li> <li>(ii) Usual care</li> </ul>	6 months	Unclear	P + HCP	60	65	MA, BP
De Souza, <sup>15</sup> Brazil	57	(i) SMBP (ii) Usual care	6 and 12 months	At least twice a week, at random times and quiet place	٩	60	NR	MA, D, PA, BP
Düsing, <sup>16</sup> Germany/ Switzerland	206	<ul> <li>(i) SMBP, education (print/online materials), medication titration protocol, adherence reminders, and physicians education</li> <li>(ii) Control</li> </ul>	34 weeks (9 months)	Unclear	P + HCP	51	46	MA/MP, BP
Fikri-Benbrahim, <sup>17</sup> Spain	180	<ul> <li>(i) SMBP, education (verbal), and education (print/ 6 months online materials)</li> <li>(ii) Usual care</li> </ul>	6 months	At least 1 day per week, on 2 occasions measure BP over 5 consecutive days	P + HCP	62	63	MA, BP, AI
Friedman, <sup>18</sup> USA	299	(i) SMBP and telemedicine (ii) Usual care	6 months	Weekly	P + HCP	17	17	MA, BP
Green, <sup>19</sup> USA	101	(i) SMBP and education (verbal) (ii) Usual care	6 months	3 days per week	P + HCP	57	42	MA, D, PA, BP
Haynes, <sup>20</sup> Canada	39	(i) SMBP and education (verbal) (ii) Control (no intervention)	6 months	Daily	٩	R	0	MA, BP
Hosseininasab, <sup>21</sup> Iran	196	(i) SMBP (ii) Usual care	4, 12, 24 weeks (1, 3, 6 months)	Daily )	۵	59	61	MA, BP
Johnson, <sup>22</sup> Canada	136	(i) SMBP (ii) Control (no intervention)	6 months	Daily	P + HCP	53	40	MA, BP, AI
Kirscht, <sup>23</sup> USA	417	(i) SMBP (ii) Control (no intervention)	2 weeks	Twice daily	P 7	78% >50	NR	MA, D
Magid, <sup>24</sup> USA	338	<ul> <li>(i) SMBP, telemedicine, education (verbal), and medication titration protocol</li> <li>(ii) Usual care</li> </ul>	6 months	3-4 times weekly	P + HCP	66	35	MA, BP, AI
Marquez-Contreras, <sup>25</sup> Spain	200	(i) SMBP (ii) Usual care	6 months	3 days a week, twice AM, twice PM	٩	59	49	MA, BP
McKenney, <sup>26</sup> USA	20	(i) SMBP (ii) Control (no intervention)	12 weeks (3 months)	Unclear	٩	75	59	MA, BP
McManus, <sup>27</sup> UK	441	(i) SMBP (ii) Usual care	6 and 12 months Monthly	Monthly	P + HCP	63	53	D, PA, BP
Mehos, <sup>28</sup> USA	41	(i) SMBP (ii) Control (no intervention)	6 months	Daily in morning	P+HCP 42% >50	2% >50	20	MA, BP, AI
Midanik, <sup>29</sup> USA	204	(i) SMBP (ii) Usual care	12 months	Twice weekly	P+HCP	47	53	D, PA, BP, AI
Migneault, <sup>30</sup> USA	337	(i) SMBP, telemedicine and education (verbal) (ii) Control (education only)	8 and 12 months Weekly	Weekly	P+HCP	57	20	MA, D, PA, BP, Al
								(Continued)

Table 1. Characteristics of included studies

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Table	

Study id, Country	Number of participants	f s Study arms included in review	Follow-up	SMBP protocol	Target <sup>a</sup>	Age	% Female	Outcomes <sup>b</sup>
Niiranen, <sup>31</sup> Finland	229	(i) SMBP and education (verbal) (ii) Control (no intervention)	12 months	Four times per year, twice in AM on 4 consecutive days	P+HCP	38	55 [	D, PA, BP, AI
Ogbuokiri, <sup>32</sup> Nigeria	29	(i) SMBP (ii) Control (no intervention)	5 months	Unclear	٩	47	85 N	MA, BP
Ogedegbe, <sup>33</sup> USA	1,039	<ul> <li>(i) SMBP, education (verbal), education (print/ online materials) and physician education</li> <li>(ii) Usual care</li> </ul>	6 and 12 months	6 and 12 months Twice daily, 3 times per week	P + HCP	56	72 N	MA, BP, AI
Rinfret, <sup>34</sup> Canada	223	<ul> <li>(i) SMBP, telemedicine and education (print/ online materials)</li> <li>(ii) Usual care</li> </ul>	12 months	Weekly	P+HCP	56	46 N	MA, BP
Rudd, <sup>35</sup> USA	150	<ul> <li>(i) SMBP, education (verbal), education (print/ online materials) and medication titration protocol</li> <li>(ii) Usual care</li> </ul>	6 months	Twice daily	P + HCP	60	53 N	MA, BP
Stewart, <sup>36</sup> Australia	395	<ul> <li>(i) SMBP, education (verbal) and adherence reminders</li> <li>(ii) Usual care</li> </ul>	6 months	Unclear	P + HCP	67	49 N	MA, BP
Van Onzenoort, <sup>37</sup> Netherland	430	(i) SMBP and medication titration protocol (ii) Control (office measures)	12 months	Monthly (before study visit), 7 consecutive days, 3 times AM and PM	P + HCP	55	45 N	MA, BP, AI
Vrijens, <sup>38</sup> Belgium	628	(i) SMBP and education (verbal) (ii) Control (no intervention)	6 weeks	Daily in AM	٩	NR	NR	MA
Wakefield, <sup>39</sup> USA	302	<ul> <li>(i) SMBP, telemedicine, education (print/online materials)</li> <li>(ii) Usual care</li> </ul>	6 and 12 months Daily	Daily	P + HCP	67	2	MA, BP, AI
Zarnke, <sup>40</sup> Canada	31	(i) SMBP and medication titration protocol (ii) Usual care	8 weeks (2 months)	Twice daily	P + HCP	55	65 N	MA, D, BP
Abbreviation: SMBF	<sup>2</sup> . self-monit	Abbreviation: SMBP. self-monitoring of blood pressure.						

Abbreviation: SMBP, self-monitoring of blood pressure. <sup>a</sup>Target of intervention: P = patient only; P + HCP = patient and healthcare professional. <sup>b</sup>Outcomes: MA = medication adherence; MP = medication persistence; PA = physical activity; D = diet; BP = blood pressure; AI = adherence to intervention

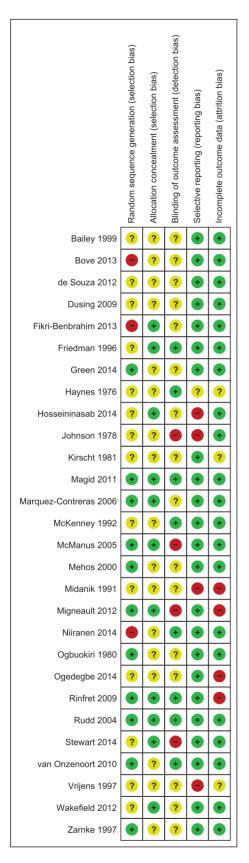


Figure 2. Risk of bias summary.

Physical activity was measured in 6 studies; 1 of these showed an increase in mean energy expenditure,<sup>30</sup> but the other 5 were negative.<sup>15,19,27,29,31</sup>

#### **Blood pressure**

Medication adherence and BP outcomes were measured together in 23 studies (all but<sup>23,27,29,31,38</sup>). In the 8 trials where SMBP had a significant effect on medication adherence, office DBP improved in 3 (38%).<sup>17,25,35</sup> Similarly, office SBP significantly improved in favor of the intervention in 3 of the 7 studies where adherence was significantly improved (43%).<sup>17,25,35</sup>

Interestingly office SBP significantly improved in 3 of 15 studies (20%) where SMBP interventions had no report effect on medication adherence,<sup>24,34,36</sup> as did office DBP in 2 of 14 studies (14%).<sup>28,34</sup>

Figure 4 shows the results of pooled analysis of DBP at 6 months, which demonstrate a significant overall effect in favor of SMBP (weighted mean differences –2.02, 95% CI –2.93, –1.11; 11 studies), with low heterogeneity ( $I^2 = 0\%$ ). A test for subgroup differences did not show a significant effect when studies were grouped according to whether medication adherence was improved or not ( $\chi 2 = 0.11$ , df = 1, P = 0.74). Results for SBP at 6 months were similar. Full BP results are available in the Supplementary Appendices S3, S4 and S5.

Exploratory meta-regression demonstrated a trend for an association between increased medication adherence and BP change (SBP and DBP); however, the results were not statistically significant, potentially due to the lack of sufficient studies.

#### DISCUSSION

#### Main results and clinical implications

This review to our knowledge is the first to carry out a pooled analysis of the effect of SMBP interventions on medication adherence, and has shown a small but significant effect (SMD = 0.21 (95%CI 0.08-0.34)).<sup>41</sup>

A recent review estimated that 59% of people with hypertension had good adherence to medication, and that around 9% of cardiovascular events could be attributed to poor adherence to medication.<sup>42</sup> Another study estimated the reduction in healthcare costs potentially associated with increasing medication adherence in hypertension in 5 European countries.<sup>43</sup> In England, it was estimated that an increase in the proportion of patients adherent to treatment to 70% (i.e., 70% taking >80% of their medication), would lead to 6,553 fewer cardiovascular events, and savings of up to €36 billion over 10 years.<sup>43</sup> The costs of nonadherence to

			Ľ	Result	
Study ID	Description	Follow-up	Intervention	Control	Between group difference?
Outcome using electronic monitoring	onic monitoring				
Düsing <sup>16</sup>	MEMS cap monitors time and date of opening pill bottle: (i) taking meds daily between 07:00 and 11:00, (ii) taking meds daily with no time restriction	9 months	(i) 57% (ii) 86%	(i) 54% (ii) 77%	(i) <i>N</i> ( <i>P</i> value not reported) (ii) <i>N</i> ( <i>P</i> value not reported)
Marquez-Contreras	Marquez-Contreras <sup>25</sup> MEMS cap monitors. (i) Proportion of doses taken, (ii) proportion of correct days, (iii) correct time, and (iv) proportion of patients who were adherent (taking 80–100% of meds)	6 months	(i) 93.5% (SD 15.7) (ii) 89.4% (SD 15.2) (iii) 88.1% (SD 21.6) (iv) 92% (SD 14.2)	(i) 87.7% (SD 23.6) (ii) 83.7% (SD 23.3) (iii) 79.9 (SD 28.2) (iv) 74% (SD 18.2)	(i) $Y (P = 0.0001)$ (ii) $Y (P = 0.0001)$ (iii) $Y (P = 0.006)$ (iv) $Y (P = 0.006)$
Rudd <sup>36</sup>	MEMs cap. Daily adherence is defined as the number of days where patients took the correct dose	6 months	80.5 (SD 23.0)	62.9 (SD 31.1)	Y (P = 0.03)
Van Onzenoort <sup>37</sup>	MEMs caps used in a single centre sub study: (i) proportion of days with correct dosing and (ii) proportion adequately adherent (>85%)	12 months	(i) 92.3% (IQR 86.9–94.4) (ii) 81%	(i) 90.9% (IQR 92.9–93.7) (ii) 74%	(i) $Y(P = 0.043)$ (ii) $N(P$ value not reported)
Vrijens <sup>38</sup>	MEMs caps. Average number of pills taken in the last week of the study (maximum of 7)	6 weeks	6.78	6.20	N (P value not reported)
Outcome using pill count	unt				
Bailey <sup>13</sup>	Proportion of available medication taken	2 months	88% (SD 27.4)	94% (SD 21.2)	N (P value not reported)
Fikri-Benbrahim <sup>17</sup>	Proportion adherent (taking 80–110% of available medication)	6 months	96.5%	85.4%	Y ( <i>P</i> = 0.011)
Friedman <sup>18</sup>	Mean change from baseline in proportion of available medication taken	6 months	+2.4%	-0.4%	N (P = 0.29)
Haynes <sup>20</sup>	Mean change from baseline in proportion of available medication taken	6 months	+21.3% (SD 29.1)	-1.5% (SD 33 1)	Y (P = 0.025)
Hosseininasab <sup>21</sup>	Proportion of available medication taken	1, 3, 6 months	1 month: 99.6% (SD 3) 3 months: 98.9% (SD 5) 6 months: 99.0% (SD 5)	1 month: 97.1% (SD 9) 3 months: 96.5% (SD 7) 6 months: 97.8% (SD 3)	Y ( <i>P</i> = 0.01) Y ( <i>P</i> = 0.005) Y ( <i>P</i> = 0.04)
Johnson <sup>22</sup>	<ul> <li>Mean change from baseline in adherence and adherence at follow-up, (ii) estimated by comparing pills on hand with pharmacy dispensing records</li> </ul>	6 months	(i) +11.8% (SD 31.5) (ii) 78.0 (SD 31.5)	(i) +1.0% (SD 40.8) (ii) 68.5 (SD 42.6)	(i) <i>N</i> ( <i>P</i> value not reported) (ii) <i>N</i> ( <i>P</i> value not reported)
McKenney <sup>26</sup>	Overall study adherence	3 months	100.2% (SD 7.0)	93.6% (SD 8.7)	Y (P = 0.02)
Van Onzenoort <sup>37</sup>	Overall study adherence	12 months	87.3%	88.1%	N (P = 0.62)
Outcome using pharmacy fill	lacy fill				
Kirscht <sup>23</sup>	Pharmacy data was used to estimate the doses of medication prescribed compared to doses dispensed	2 weeks	66.5%	66.5%	N (P value not)
Magid <sup>24</sup>	Medication possession ratio (MPR) total number of days supplied for each medication, divided by period for which the medication was prescribed	6 months	0.85 (SD 0.19)	0.84 (SD 0.19)	N (P = 0.88)
					(Continued)

Table 2. Effect of SMBP on medication adherence

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			Re	Result	
Study ID	Description	Follow-up	Intervention	Control	Between group difference?
Mehos <sup>28</sup>	Overall study compliance (no. tablets refilled/ amount prescribed)	6 months	82%	89%	N (P = 0.29)
Ogbuokiri <sup>32</sup>	Frequency of refill. Value arbitrarily chosen and defined prestudy (refill within 1–10 days of refill date = 100%; within 2 weeks = 50%; within 4 weeks = 25%)	5 months	72.6%	59.26%	NA
Rinfret <sup>34</sup>	(i) Continuous medication availability (CMA) and (ii) continuous medication gaps (CMG) scores, which estimate the proportion of time the subjects have or do not have medication available	12 months	(i) 0.95 (IQR 0.76 to 1.00) (ii) 0.04 (IQR 0.00–0.19)	(i) 0.91 (IQR 0.54–1.04) (ii) 0.09 (IQR 0.00–0.38)	(i) $N(P = 0.07)$ (ii) $N(P = 0.12)$
Stewart <sup>36</sup>	Follow-up mean and mean change from baseline in: (i, ii) MedsIndex score (100 = perfect adherence); (iii, iv) Medication Possession Ratio	6 months	(i) 84.75 (SD 17.13) (ii) +4.60 (iii) 0.94 (SD 0.35) (iv) +0.13	(i) 82.86 (SD 19.42) (ii) +2.44 (iii)0.89 (SD 0.21) (iv) +0.08	(i) NR (ii) N (P = 0.228) (iii) NR (iv) N (P = 0.496)
Outcome using self-report	eport				
Bove <sup>13</sup>	Medication adherence self- efficacy scale (MASES). Four-item scale, higher scores indicate greater level of adherence	6 months	3.56 (SD 0.81)	3.59 (SD 0.85)	N (P = 0.86)
De Souza <sup>15</sup>	Proportion of patients who reported "regular use daily" of antihypertensive medication	6 and 12 months	6 months: 94.7% 12 months: 100%	6 months: 83.3% 12 months: 88.2%	6 months: $N (P = 0.150)$ 12 months: $Y (P = 0.031)$
Green <sup>19</sup>	Mean change from baseline in Morisky 8-item score. Higher score indicates lower adherence	6 months	-0.1 (SD 2.0)	-0.2 (SD 1.9)	N (P = 0.79)
Kirscht <sup>23</sup>	Patients were asked about pill taking behaviour and were ranked on an ordinal scale	2 weeks	94.4%	94.3%	N (P value not reported)
Migneault <sup>30</sup>	Mean change from baseline in Morisky 7 score. Higher scores indicate better adherence	8 months	+0.45	+0.26	N (P value not reported)
Ogedegbe <sup>33</sup>	Mean change in Morisky 4-item score. Higher score indicates poor adherence	6 and 12 months	6 months: -0.14 12 months: -0.24	6 months: -0.13 12 months: -0.20	6 months: $N (P = 0.87)$ 12 months: $N (P = 0.71)$
Stewart <sup>36</sup>	<ul> <li>(i, ii) Follow-up mean and mean change from baseline in proportion adherent using Morisky 4; (iii, iv) Morisky 4 score (0 = good adherence); (v, vi) TABS differential (&gt;15 = good adherence)</li> </ul>	6 months	(i) 73.5% (ii) +13.5% (iii) 0.36 (SD 0.67) (iv) -0.20 (v) 11.10 (SD 3.83) (vi) +0.85	(i) 63.6% (ii) +6.4% (iii) 0.44 (SD 0.64) (iv) -0.15 (v) 11.59 (SD 3.33) (vi) +0.67	(i) $N$ ( $P = 0.09$ ) (ii) $N$ ( $P$ value not reported) (iii) $NR$ (iv) $N$ ( $P = 0.310$ ) (v) $NR$ (v) $N$ ( $P = 0.856$ )
Wakefield <sup>39</sup>	Patients were asked, "are you taking your medications as prescribed". Scores represent the proportion of medications for which responses agreed with the directions for use on the VA pharmacy medication profile	6 and 12 months	6 months: 99.8 (SD 1.4) 12 months: 99.7% (SD 1.4)	6 months: 99.6 (SD 2.2) 12 months: 98.9% (SD 6.0)	6 months: $N (P = 0.79)$ 12 months: $N (P = 0.20)$
Zarnke <sup>40</sup>	Mean number of self-reported doses missed per week	2 months	0.05 (SD 0.2)	0.2 (SD 0.4)	N (P value not reported)
			C		

Table 2. Continued

Abbreviation: SMBP, self-monitoring of blood pressure; MEMS, medication event monitoring system; IQR, interquartile range; NR, not reported; VA, Veterans Affairs. 7207 ludY 2L uo tsen6 Ad 66L5427/607L/0L/8Z/alpitu/qib/uoo:dno:pimepeze//:sdtty would pepeolumod

		SMBP			ontrol			Std. Mean Difference	Std. Mean Difference
Study or Subgroup		SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
1.1.1 Electronic monitori	ng								
Marquez-Contreras 2006		15.2	100		23.6	100	10.5%	0.29 [0.01, 0.56]	
Rudd 2004	80.5	23	69	62.9	31.1	68	8.4%	0.64 [0.30, 0.98]	
Subtotal (95% CI)			169			168	18.8%	0.45 [0.10, 0.79]	-
Heterogeneity: Tau <sup>2</sup> = 0.04 Test for overall effect: Z = 2				P = 0.12	;  ² =	59%			
	2.34 (F -	- 0.01)							
1.1.2 Pill count									
Bailey 1999	88	27.4	30	94	21.2	28	4.8%	-0.24 [-0.76, 0.28]	
Haynes 1976	65.8	36.7	20	43.2	42.9	18	3.4%	0.56 [-0.09, 1.21]	+
Hosseininasab 2014	99	5	94	97.8	3	96	10.2%	0.29 [0.00, 0.58]	
Johnson 1978	78	31.5	34	65.5	42.6	34	5.4%	0.33 [-0.15, 0.81]	+
McKenney 1992	100.2	7	17	93.6	8.7	17	2.9%	0.82 [0.11, 1.52]	
Subtotal (95% CI)			195			193	26.8%	0.30 [0.01, 0.59]	<b>•</b>
Heterogeneity: Tau <sup>2</sup> = 0.04				P = 0.14	);  ² = -	42%			
Test for overall effect: Z = 2	2.04 (P =	= 0.04)							
1.1.3 Pharmacy fill									
Magid 2011	0.85	0.19	112	0.84	0.19	112	11.1%	0.05 [-0.21, 0.31]	
Stewart 2014	0.94	0.35	174	0.89	0.21	151	12.8%	0.17 [-0.05, 0.39]	
Subtotal (95% CI)			286			263	23.9%	0.12 [-0.05, 0.29]	•
Heterogeneity: Tau <sup>2</sup> = 0.00				P = 0.50	);  ² =	0%			
Test for overall effect: Z =	1.42 (P =	= 0.15)							
1.1.4 Self report									
Bove 2013		0.81	99		0.85	107	10.6%	-0.04 [-0.31, 0.24]	
Green 2014	0.1	2	44	0.2	1.9	46	6.7%	-0.05 [-0.46, 0.36]	
Wakefield 2012	99.8	1.4	102	99.6	2.2	107	10.7%	0.11 [-0.16, 0.38]	
Zarnke 1997	6.95	0.2	20	6.8	0.4	10	2.5%	0.52 [-0.25, 1.29]	
Subtotal (95% CI)			265			270	30.5%	0.05 [-0.13, 0.22]	<b>—</b>
Heterogeneity: $Tau^2 = 0.00$ Test for overall effect: Z = 0				P = 0.53	);  ² =	0%			
resciol overall effect: Z = 1	0.52 (P =	- 0.00)							
Total (95% CI)			915				100.0%	0.21 [0.08, 0.34]	· · · · · · · · · · · · · · · · · · ·
Heterogeneity: Tau <sup>2</sup> = 0.02	,			2 (P = 0	05); l²	= 43%		+-2	· -1 0 1
Test for overall effect: Z = 3			/					2	Favours control Favours SMBP
Test for subgroup difference	ces: Chi <sup>2</sup>	= 5.47	', df = 3	(P = 0.	14), l <sup>2</sup>	= 45.1	%		

Figure 3. Self-monitoring of blood pressure interventions vs. controls for antihypertensive medication adherence.

antihypertensives in the United States has been estimated to be as much as \$105 billion annually.<sup>44</sup>

Only one study in the review included evidence on medication persistence. Helping patients take their medication correctly on a day-to-day basis is important (adherence), but in conditions that require long-term treatment such as hypertension, making sure patients keep taking the medication over time (persistence) is of equal if not greater importance. Meta-analysis shows that the effect of antihypertensive treatment is apparent within a year and ongoing risk reduction is dependent on ongoing treatment.<sup>45</sup>

Importantly, studies using more objective measures of medication adherence showed a greater effect size in favor of intervention. The pooled estimate when electronic monitoring was used was almost double the overall estimate, and approaching 10 times larger than the estimate from studies where the least objective self-reported measures were used. Objective measurement may remove the measurement noise associated with self-report, therefore making more precise estimates of adherence possible hence easier differentiation between low and high adherence.

While SMBP has been shown to improve medication adherence, the results of this review do not provide evidence that this explains all of the observed BP reduction. Further research is needed to clarify whether this is because the effect of SMBP is not mediated by medication adherence, or due to methodological issues such as the sensitivity of outcome measures and use of cointerventions targeting other behaviors.

There is insufficient evidence from randomized controlled trials testing the effect of SMBP on lifestyle factors to be able to draw any conclusions about the extent to which they may mediate the effect of SMBP.

#### **Comparison to the literature**

The effect of SMBP on medication adherence shown in this review compares favorably with other interventions aimed at improving adherence. Evidence from a review of interventions to improve medication adherence in hypertensives carried out in 2004 showed a small and nonsignificant overall effect, SMD = 0.12 (95% CI –0.06 to 0.28).<sup>46</sup> A meta-analysis of trials to improve medication adherence in any condition reported a small but significant effect, SMD = 0.08 (95% CI 0.04–0.12).<sup>47</sup>

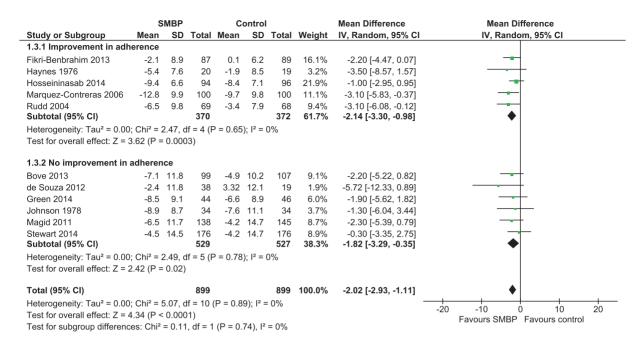
#### Strengths and weaknesses

This review used a comprehensive search strategy and captured more than double the number of studies compared to previously.<sup>7</sup> Sufficient data were available to perform meta-analysis for medication adherence allowing estimation of the effect size.

			Re	Results	
Study i.d.	Outcome measure	Follow-up	Intervention	Control	Difference between groups?
Medication persistence	srsistence				
Düsing <sup>16</sup> Diet	Proportion not discontinuing medication by end of trial	9 months	95.9%	88.3%	N (P value not reported)
De Souza <sup>15</sup>	De Souza <sup>15</sup> Proportion reporting food intake according to dietary quidelines	6 and 12 months	6 months: 97.4% 12 months: 97.3%	6 months: 88.9% 12 months: 100%	6 months: <i>N</i> ( <i>P</i> = 0.21) 12 months: <i>N</i> ( <i>P</i> = 0.68)
Green <sup>19</sup>	Mean change from baseline in average number of daily servings of fruit and vegetables	6 months	+2.3 (SD 3.0)	+0.0 (SD 1.9)	Y (P < 0.01)
Kirscht <sup>23</sup>	Proportion adherent to dietary recommendations	2 weeks	75.2%	77.2%	N (P value not reported)
McManus <sup>27</sup>	Mean change from baseline in: (i) proportion adding salt to food and (ii) proportion drinking more than recommendations (men >21; women >14 units/ week)	6 and 12 months	6 months: (i) -2%, (ii) -8% 12 months: (i) -4%, (ii) -6%	6 months: (i) -2%, (ii) -3% 12 months: (i) +3%, (ii) -2%	6 months: (i) $N (P = 0.82)$ , (ii) $N$ ( $P = 0.11$ ) 12 months: (i) $Y (P = 0.03)$ , (ii) $N$ ( $P = 0.56$ )
Midanik <sup>29</sup>	(i) Mean change in alcohol consumption (drinks per day) and (ii) coffee consumption (drinks per day)	12 months	(i) -0.2 (SD 0.9) (ii) -0.1 (SD 1.4)	(i) -0.2 (SD 0.8) (ii) -0.5 (SD 1.4)	(i) $N (P = 0.87)$ (ii): $N (P = 0.05)$
Migneault <sup>30</sup>	<ul> <li>Mean change from baseline in overall diet quality score (higher score = healthier diet)</li> </ul>	8 months	+2.8	-0.74	Y (P < 0.05)
Niiranen <sup>31</sup>	<ul> <li>(i) Mean change from baseline in: alcohol intake (g/ day); (ii) total energy intake (MJ/day); (iii) total carbohydrate (%MJ/day); (iv) total protein (%MJ/ day); (v) total fat (%MJ/day); (vi) total saturated fat (%MJ/day)</li> </ul>	12 months	(i) -0.1 (SD 8.2) (ii) -0.3 (SD 1.8) (iii) +1.5 (SD 6.3) (iv) +0.0 (SD 1.8) (v) -0.8 (SD 6.1) (vi) -0.7 (SD 2.6)	(i) +3.2 (SD 16.5) (ii) -0.1 (SD 1.3) (iii) +0.0 (SD 6.7) (iv) +0.7 (SD 2.6) (v) -0.2 (SD 2.1) (vi) -0.7 (SD 2.6)	(i) $N (P = 0.06)$ (ii) $N (P = 0.37)$ (iii) $N (P = 0.10)$ (iv) $N (P = 0.12)$ (v) $N (P = 0.12)$ (v) $N (P = 0.11)$ (vi) $N (P = 0.11)$
Zarnke <sup>40</sup>	Mean change from baseline in alcohol intake (drinks per week)	2 months	-0.25 (SD 1.59)	+0.10 (SD 0.4)	N (P value not reported)
Physical activity	ity				
De Souza <sup>15</sup>	De Souza <sup>15</sup> Proportion exercising more than 3 times weekly	6 and 12 months	6 months: 67.6% 12 months: 67.6%	6 months: 61.1% 12 months: 58.8%	6 months: <i>N</i> ( <i>P</i> = 0.22) 12 months: <i>N</i> ( <i>P</i> = 0.19)
Green <sup>19</sup>	Proportion at follow-up engaging in physical activity (often working up a sweat)	6 months	27.9% (SD 44.1)	20.5% (SD 40.2)	<i>N</i> ( <i>P</i> = 0.40)
McManus <sup>27</sup>	Mean change from baseline in proportion exercising more than 3 times weekly	6 and 12 months	6 months:+9% 12 months: +4%	6 months: +13% 12 months: +3%	6 months: <i>N</i> ( <i>P</i> = 0.53) 12 months: <i>N</i> ( <i>P</i> = 0.49)
Midanik <sup>29</sup>	Physical activity at follow-up (*study reported no difference between groups, but reported no data)	12 months	Not reported	Not reported	N (P value not reported)
Migneault <sup>30</sup>	<ul> <li>(i) Mean change from baseline in: moderate or greater intensity activity time (min/week), (ii) proportion exercising &gt;150 min/week, and (iii) total energy expenditure (kcal/day)</li> </ul>	8 months	(i) -3.44, (ii) -2%, (iii) +43.8	(i) +2.77, (ii) +5%, (iii) -36.2	<ul> <li>(i) N (P value not reported), (ii) N (P value not reported) (iii) Y (P &lt; 0.05)</li> </ul>
Niiranen <sup>31</sup>	Mean change from baseline in leisure activity (MJ/day)	12 months	+0.00 (SD 0.4)	+0.07 (SD 0.3)	<i>N</i> ( <i>P</i> = 0.15)

Abbreviation: SMBP, self-monitoring of blood pressure.

 Table 3
 Effect of SMBP on lifestyle factor outcomes





Overall, the quantity and quality of evidence of the impact of SMBP on lifestyle factors was poor. Evidence for the effect of SMBP on diet and physical activity was available in only 9 studies, and where significant effects in favor of the intervention were found, few were clinically significant. UK guidance for the management of hypertension recommends that lifestyle advice should be offered to all people undergoing treatment for hypertension. SMBP could potentially act by helping hypertensives see the benefits of a healthier lifestyle, but more data are required before this can be substantiated.

The interventions tested were heterogeneous, with varying target population, SMBP protocol, medication titration protocol, and other cointerventions. Studies were often aimed at people with hypertension, but also required the input of HCPs to interpret the SMBP measurements and act accordingly. Using complex interventions and targeting both patients and HCPs together complicate the investigation of the independent effect of SMBP on patient behavior. Further work should specifically examine the effect of SMBP on physician behavior, e.g., prescribing, and the extent to which this could be a mediator.

The theoretical basis for intervention development only reported in 4 studies (14%). As SMBP interventions target behavior change in patients and/or HCPs, conceptual models are needed to provide a framework for the development of interventions. As it stands, it is difficult to understand how many SMBP interventions have been developed, e.g., the justification for the frequency of SMBP and what patients/ HCPs are expected to do with these readings.

#### CONCLUSIONS

SMBP leads to an increase in medication adherence, and best seen in those studies where objective measures are used. However, to what extent medication adherence acts as a mediator of the effect of SMBP remains to be determined. The role of lifestyle factors is less clear, and it is feasible and indeed likely, that other mediators may affect the outcomes of SMBP such as physician prescribing.

Furthermore, future trials should ideally use methods that allow for the potential incremental effects of cointerventions to be determined (e.g., using a multifactorial design). More transparency is needed in reporting the basis of the intervention development. SMBP improves adherence to medication as well as lowering BP, however a better understanding of the mediators of these effects is needed, in order to optimize SMBP interventions for translation to the "real-world".

#### SUPPLEMENTARY MATERIAL

Supplementary materials are available at American Journal of Hypertension (http://ajh.oxfordjournals.org).

#### ACKNOWLEDGMENTS

R.J.M. has received research funding from Omron and Lloyds Pharmacies in terms of blood pressure monitoring equipment.

#### DISCLOSURE

B.R.F., J.H.B., and L.H. declare no conflicts of interest.

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