



# Self-monitoring of blood pressure to guide titration of antihypertensive medication – a new era in hypertension management?

Jan K. Ho<sup>1</sup>, Revathy Carnagarin<sup>1</sup>, Vance B. Matthews<sup>1</sup>, Markus P. Schlaich<sup>1,2,3</sup>

<sup>1</sup>Dobney Hypertension Centre, School of Medicine - Royal , Perth Hospital Unit/Medical Research Foundation, University of Western Australia, Crawley WA, Australia; <sup>2</sup>Departments of Cardiology and Nephrology, Royal Perth Hospital, Perth, Australia; <sup>3</sup>Neurovascular Hypertension & Kidney Disease Laboratory, Baker Heart and Diabetes Institute, Melbourne, Australia

*Correspondence to:* Markus P. Schlaich. Dobney Chair in Clinical Research, School of Medicine - Royal Perth Hospital Unit, The University of Western Australia, Level 3, MRF Building, Rear 50 Murray St, Perth WA 6000, Australia. Email: markus.schlaich@uwa.edu.au.

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Hypertension remains the leading modifiable risk factor for cardiovascular morbidity and mortality worldwide and accounts for more than 10 million deaths annually (1). Despite the availability of effective pharmacotherapy, control rates of hypertension remain less than 50% in most countries. International data suggest that only half of affected subjects are aware of their elevated blood pressure (BP) and less than a third of patients receiving antihypertension treatment actually reach target BP levels (2). Indeed, the recently published data from May Measurement Month 2017, a global BP screening and awareness campaign initiated by the International Society of Hypertension, collected BP data obtained from more than 1.2 million subjects across 80 countries in a standardized fashion and revealed a global prevalence of hypertension (elevated BP >140/90 mmHg or on antihypertensive therapy) in 34.9% of the adult population (3). Moreover, 46.3% of patients who were treated for their hypertension had BP levels above 140/90 mmHg and hence remained uncontrolled, thereby leaving these patients at increased CV risk (3). Suboptimal prescribing practices, the lack of awareness and difficulty obtaining reliable BP measurements are some of the factors contributing to suboptimal BP control. Increased use of out-of-office BP measurements, particularly 24-hour ambulatory blood pressure monitoring (ABPM) is crucial in obtaining more reliable BP measures

and is increasingly being recognized to provide additional prognostic value and guidance for adequate treatment (4). Similarly, there is increasing evidence for additional benefit for home BP monitoring. In this context, the recently published TASMINH4 trial assessing the efficacy of self-monitored BP, with or without telemonitoring, for titration of anti-hypertensive medication has potential wide ranging implications for future management of hypertension in clinical practice (5).

The TASMINH4 trial enrolled 1,182 patients with hypertension from 142 general practices in the UK with 393, 394 and 395 patients assigned to the telemonitoring group, usual care group and self-monitoring group, respectively. The groups were largely well matched at baseline, with a mean age of 66.9±9.4 years (SD), mean BP of 153.1±14.0/85.5±10.3 mmHg, and a mean elapsed time of 10.2±8.4 years since diagnosis of hypertension.

Over the 12-month period whereby the treating doctors had complete medical therapeutic liberty, patients were treated to their pre-defined target BP of 140/90 mmHg for patients aged below 80 years, 150/90 mmHg for patients aged 80 years and above, and less than 140/80 mmHg for patients with diabetes. At the end of the 12 months period, patients in the telemonitoring and self-monitoring group had meaningful, statistically significant reductions in mean

systolic BP of 4.7 (2.4–7.0) and 3.5 (1.2–5.8) mmHg, respectively.

In the TASMINH4 study, self-monitoring patients were taught to use a validated automated electronic sphygmomanometer, measuring their own BP twice each morning and evening for the first week, with recommendations for titration of medication made by their general practitioners (GP) based upon these readings. The telemonitoring patients delivered their BP measurements via a short messaging service, with an algorithm to alert patients to contact their GPs with extreme readings. Importantly, the telemonitoring patients were reminded to contact their GPs if they did not provide adequate readings or if their BP was suboptimal. The patients that underwent usual care had their anti-hypertensive medications titrated according to their clinic BP measurements at the discretion of their GPs.

Fifty percent of all patients assessed initially were excluded from the study due to controlled BP (1,048 patients), orthostatic hypotension (86 patients), or the lack of stable anti-hypertensive medication (22 patients). Fifty-three percent of patients were male and most patients were of Caucasian ethnicity.

The telemonitoring patients achieved a statistically significant reduction in BP earlier than the self-monitoring patient. At six month follow up the actual mean difference was  $-3.7$  mmHg when compared to the usual care patient group. The self-monitoring patients achieved a mean reduction of  $-2.1$  mmHg with a clear trend towards statistical significance ( $P=0.0584$ ). These reductions would eventually become significant at the 12-month follow up.

Notably, the patients in the self-monitoring group and telemonitoring group were treated with slightly more medications than their usual care counterparts with an adjusted mean difference (AMD) of 0.11 ( $P=0.0129$ ) for the self-monitoring group and 0.13 ( $P=0.0038$ ) for the telemonitoring group when compared to the usual care group. Likewise, there was an increase in the defined daily doses (DDD) at 12 months in the telemonitoring group with an AMD of 0.31 ( $P<0.0001$ ) but not in the self-monitoring group (AMD of 0.19) when compared to usual care. There were no significant differences in adherence between the groups which were measured with a self-reported medication adherence rating scale (MARS). The increase in the DDD was largely due to increases in angiotensin-converting-enzyme inhibitors and angiotensin receptor blockers.

The mean improvement in BP at 12 months *vs.* usual

care was 4.7 and 3.5 mmHg in the telemonitoring and self-monitoring group, respectively with a non-significant difference of 1.2 mmHg between the two intervention groups. Given the absence of an increase in the DDD of medications in the self-monitoring group the improvement in BP by 3.5 mmHg may have been driven mainly by an increase in the number of medications [AMD of 0.11 (95% CI, 0.02–0.19);  $P=0.0129$  *vs.* control group]. Overall, the BP lowering effect in both intervention groups was largely attributed to the increase in number of medications and daily defined doses but other factors may also have contributed. For example, as pointed out by the investigators, the MARS may not have been sensitive enough to detect subtle differences in medication adherence.

Overall, this study suggests that involvement of patients in their care through self-monitoring with and without telemonitoring appears to have beneficial effects compared to current usual care approach and results in better BP control. This is an important finding and may well have implications on how BP should be monitored and medication titrated in general practice. However, despite the clear merits of this study, several issues require further consideration and clarification in future studies.

### Role of target BP

BP thresholds for the diagnosis of hypertension are based upon the different methods of measurements, i.e., clinic, home, or 24-hour ambulatory BP measurement. Current guidelines define hypertension as more than 140/90 mmHg with clinic BP measurement, more than 130/80 mmHg with 24-hour ambulatory BP measurement, or more than 135/85 mmHg with home BP measurements (4,6). These criteria reflect the equivalence of BP levels based on the mode of measurements and their association with cardiovascular risk. The studies by Niiranen *et al.* and Kikuya *et al.* demonstrated that a home BP of 133.4/82.2 mmHg and a 24-hour ABP measurement of 131/79.4 mmHg matched the cardiovascular risk rates associated with a clinic BP of 140/90, which is in line with current BP recommendations for the diagnosis of hypertension (7,8).

In self-monitoring patients and telemonitoring patients in the TASMINH4 study, the primary endpoint of measured clinic systolic BP improved more than in the usual care group. It is important to note in this context that titrating of antihypertensive therapy in self-monitoring patients with or without telemonitoring was based on the lower

**Table 1** Criteria for hypertension diagnosis for various measurement modes

Mode of measurement	Systolic BP (mmHg)		Diastolic BP (mmHg)
Clinic	≥140	and/or	≥90
ABPM over 24 hours	≥130	and/or	≥80
HBPM	≥135	and/or	≥85

BP, blood pressure; ABPM, ambulatory blood pressure measurement; HBPM, home blood pressure measurement.

thresholds for home monitoring, i.e., 135/85 mmHg. While the office BP hypertension thresholds of >140/90 mmHg is considered equivalent to >135/85 mmHg with home monitoring, using these thresholds as targets below which BP should be lowered is less well established. Nevertheless, the lesson from the TASMING4 study is that target BP levels should be in line with the mode of BP monitoring used, which results in improved BP control measured either way (Table 1) (9).

### Selection bias

Selection bias remains an issue to be taken into account in this study as patients enrolled into the self-monitoring and telemonitoring groups may have higher motivation to improve their health status thereby potentially influencing the outcomes of the group although, this effect is unlikely given the randomization process. The additional alerts provided in the telemonitoring patients, however, may have been another possible source of increased motivation. The effects of close patient-physician interaction in the management of hypertension has previously been investigated by Naik and colleagues who reported better BP control in hypertensive and diabetic patients with more patient-physician interaction (10). Furthermore, the higher number of data points available with self- and telemonitoring may have resulted in more confidence and willingness to manage the elevated BP levels more aggressively and implement more timely adjustments of their anti-hypertensive medications.

### Other measures of BP

The SPRINT study clearly demonstrated that intensive BP lowering reduced primary outcomes and all-cause mortality with hazard ratios of 0.75 (P<0.001) and 0.73 (P=0.003), respectively (11). The SPRINT study utilised automated office BP measurements and raised some concern regarding the equivalence between automated office blood pressure

(AOBP) and home blood pressure (HBP) measurements against the established standard of 24-hour ABPM. However, the post SPRINT study survey by Johnson *et al.* suggested that there were no differences in measurements between attended and unattended patients (12). 24-hour ambulatory BP monitoring remains the diagnostic standard for hypertension with several meta-analysis supporting its superiority in predicting cardiovascular outcomes, risk stratification, and its ability to monitor nocturnal BP (13-15). The Ambulatory Blood Pressure Collaboration in Patients with Hypertension (ABC-H) meta-analysis of 17,312 patients demonstrated that a blunted lowering of nocturnal BP was predictive of worse outcomes, independent of their mean 24-hour BP measurements (13). Furthermore, masked hypertension, which cannot be detected with office readings, is associated with excess cardiovascular mortality risk (16). In this context, neither AOBP nor home BP measurements are ideal for the elucidation of such diagnoses (17). Most recently, Banegas *et al.* reported that ambulatory systolic BP was a stronger predictor of all-cause and cardiovascular mortality than clinic based BP measurements (18).

With regards to actual current practice of BP measurements, GPs were surveyed by Kaczorowski *et al.* who found that 54.2% of GPs performed manual BP measurements whilst 42.9% utilised AOBP measurements when screening for hypertension (19). For the diagnosis of hypertension, 31.1% of GPs relied upon AOBP measurement, followed by home BP measurement (22.4%) and manual office BP measurement (21.4%). Ambulatory BP measurement was used for diagnosis by 14.4% of responding GPs (19).

Given the potential logistical difficulty, the costs and compliance issues of 24-hour ambulatory BP measurements, AOBP measurements and HBP measurements are indeed very helpful as tools for the diagnosis of hypertension.

### Adherence with prescribed medication

In the TASMING4 study, patients self-reported their

**Table 2** Brief summary

## What the TASMINH4 study adds

- HBPM is a helpful additional tool for the diagnosis of hypertension
- HBPM may increase patient engagement and improve BP control
- Increased number of BP data may facilitate more aggressive BP management

## Limitations

- Long-term clinical outcomes associated with HBPM based management remain unclear
- HBPM is unable to assess nocturnal hypertension and dipping pattern
- HBPM depends on appropriate measuring technique by the patient

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HBPM, home blood pressure measurement; BP, blood pressure.

medication adherence using the MARS. This may be source of bias as medication adherence may not be accurately reflected. Other more accurate forms of medication monitoring like monitoring pre-packaged dosettes or electronic monitoring may have been a more accurate albeit inconvenient option. Adherence to medication therapy has been a persistent issue in the management and treatment of hypertension. Corrao *et al.* reported a 54–61% of patients having very low to low adherence to anti-hypertensive medication therapy in a nested case-control study of 76,017 patients (20). These findings are supported by work from Azizi *et al.* who investigated the prevalence of non-adherence to medical therapy in patients scheduled for renal denervation to lower BP, and found a non-adherence rate of 50% (21). To improve adherence with prescribed medications, several interventions have been trialled including motivational interviewing which resulted in improved medication adherence, as well as text-messaging support which had no significant effect (22,23). Interestingly, van Onzenoort *et al.* reported that a Medication Event Monitoring System (MEMS) did neither improve BP control nor did it impact on changes in drug use (24). Improving adherence to prescribed pharmacotherapy is likely to reduce morbidity and complications from uncontrolled hypertension. Interestingly, a recent Cluster-Randomized Trial of Blood-Pressure Reduction in Black Barbershops study by Victor *et al.* demonstrated significantly greater reduction in BP (27 *vs.* 9.3 mmHg) in a barbershop setting with trained pharmacists to prescribe medications versus controls who were encouraged to implement lifestyle modification and seek doctors' appointments (25). Criticisms of this study included the \$25 provided to patients as compensation for their travel and medication cost as a possible source of bias. Indeed, similar findings were previously reported by

Petersen *et al.* where individual financial incentives only improved BP control (26). The global issue of suboptimal management of hypertension in the community has been further highlighted by the recently published results of the May Measurement Month initiative with approximately half of the patients who were treated not reaching target BP levels (3). Similarly, Sheppard *et al.* reported that in a primary care setting 4,421 (35%) of 12,647 hypertensive patients were untreated (27).

The TASMINH4 study is an encouraging one with data to support use of self-monitoring and tele-monitoring methods for BP management. However, the short follow-up duration is cause for uncertainty relating to the efficacy and longevity, as well as cost-effectiveness beyond the time frame observed in the study. Furthermore, improvements in hard cardiovascular clinical endpoints would be reassuring to demonstrate that such interventions can be sustained and translate into cardiovascular and mortality benefits. Despite some limitations, the TASMINH4 study provides further insight into and support of the use of non-office based BP measurements as a useful guide for the diagnosis and therapy of hypertension. Nevertheless, there remains a need for continued use of adequately measured office-based BP, at least for the time being (*Table 2*).

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