OPEN

Journal of Human Hypertension (2013) **27,** 545–551

www.nature.com/jhh

ORIGINAL ARTICLE

Barriers to achieving blood pressure treatment targets in elderly hypertensive individuals

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High blood pressure (BP) is highly prevalent among the elderly, and even with pharmacological therapy BP is difficult to control to guideline recommended levels. Although poor compliance to therapy is associated with less BP control, little is known regarding other barriers to attaining on-treatment target BP. This study examined factors associated with achieving on-treatment target BP in 6010 hypertensive participants aged 65–84 years from the Second Australian National Blood Pressure study. Participants were followed for a median of 4.1 years, with BP monitored every 6 months. 'Target BP' was defined as a reduction of systolic/diastolic BP of at least 20/10 mm Hg and BP $<$160/90 mm Hg from randomization in two consecutive follow-up visits. Cox regression was used to identify factors associated with achieving target BP from a number of baseline and in-study factors. Mean BP at randomization was 168/91 mm Hg and patients had a median of 9 (range: 2–20) study visits. Target BP was achieved in 50% of patients. Demographic factors associated with achieving target BP were male gender, living in a regional area; and clinical factors included history of antihypertensive therapy, increased plasma creatinine, lower pretreatment pulse pressure and in-study use of multiple BP-lowering drugs. Those aged $>$80 years and seeking care from multiple doctors (hazard ratio 0.40, 95% confidence interval 0.36–0.45, $P<0.001$) were less likely to achieve target BP. These findings identify clinical markers that can be targeted for intervention, but also demographic factors related to service delivery, which may provide further opportunity for achieving better BP control in hypertensive elderly.

Journal of Human Hypertension (2013) **27,** 545–551; doi:10.1038/jhh.2013.11; published online 28 February 2013

Keywords: elderly; blood pressure; control; barriers; Australia

INTRODUCTION

High blood pressure (BP) is a well-established independent risk factor for cardiovascular disease morbidity and mortality, and remains one of the leading causes of death and disability worldwide.[1] In most developed, and an ever increasing number of developing nations, approximately 20 to 30% of the adult population has high BP and the prevalence increases as age advances, with rates often $>$60% in those 65 years and older.[2,3] Lowering high BP reduces the risk of cardiovascular morbidity and mortality.[4] A wealth of evidence from randomized controlled trials has established that pharmacological treatment is beneficial in achieving long-term lowering of BP, which is associated with a reduction of the risk of cardiovascular events.[5]

The level to which BP should be lowered by treatment with BP-lowering drugs (target or goal BP) has been constantly evolving over the past decades with the accumulation of evidence from large-scale, outcome-driven clinical trials. This trial evidence has been used by clinical societies and government agencies to produce guidelines for the management of high BP that form the basis of clinical management.[1,6,7] However, a number of observational studies have shown that for many people with high BP, target BP is difficult to achieve in clinical practice with current regimens of BP-lowering medication. Approximately half of the hypertensive patients taking BP-lowering medication in one Australian survey did not reach their BP targets, and this finding has been corroborated in other countries.[8,9] Achieving BP targets with BP-lowering drugs in elderly patients has been shown to be even more difficult.[10,11] Therefore, uncontrolled hypertension, despite drug treatment, remains a major public health concern worldwide.

The underlying causes of this difficulty in achieving target BPs in treated hypertensive patients are not well understood. Earlier studies showed that there are likely to be a number of patient- and physician-related factors involved including patient compliance as well as physician inertia in regards to increasing both number and dose of treatments.[12–15] Although the level of BP before treatment could be an important factor in attaining a target BP following treatment, we hypothesize that there may be a number of other demographic and clinical (patient- or lifestyle-related) factors, which are responsible for such treatment failure. The aim of this study is to identify factors associated with achieving BP targets in an elderly hypertensive population treated with BP-lowering medications.

MATERIALS AND METHODS

Study design and participants

The Second Australian National Blood Pressure (ANBP2) study was a prospective, open-label study with blinded assessment of endpoints (PROBE design), in which 6083 hypertensive patients aged 65 to 84 years

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Received 6 August 2012; revised 9 January 2013; accepted 13 January 2013; published online 28 February 2013

were randomized to either a diuretic or an angiotensin-converting enzyme inhibitor (ACE-I) based BP-lowering drug regimen. The study was conducted through the clinics of 1594 general practitioners (GPs) from five states (New South Wales, South Australia, Queensland, Victoria and Western Australia) of Australia to compare the outcome of treatment regimens. The study protocol was approved by the ethics committee of the Royal Australian College of General Practitioners and conducted in accordance with the Helsinki Declaration. Details about the study design, recruitment and BP measurement processes have been published previously.[16] In brief, inclusion in the study required an average untreated baseline systolic BP (SBP) of at least 160 mm Hg or above 140 mm Hg if the average baseline diastolic BP (DBP) was at least 90 mm Hg, no cardiovascular morbidity within last 6 months, and willingness to participate in the study. The study exclusion criteria included: any life threatening illness, contraindication to ACE-I or diuretics, plasma creatinine >2.5 mg/dl, malignant hypertension, or dementia.

Following randomization, GPs were responsible for antihypertensive therapy management while conforming to the randomized treatment allocation and BP goals. Guidelines provided to them aimed to achieve the target BP of a reduction of SBP by at least 20 mm Hg to <160 mm Hg with a further reduction to <140 mm Hg if tolerated and a reduction of DBP by at least 10 mm Hg to <90 mm Hg with a further reduction to <80 mm Hg if tolerated. To achieve goal BP, addition of beta-blockers, calcium channel blockers and alpha-blockers were recommended in both groups. In-study BP was recorded annually by study nurses and at each patient visit by the general practitioner using routine mercury sphygmomanometer until study closure, or termination; or if the patient died or withdrew from the study.

Target BP definitions

The trial definition of 'target BP achievement' was defined when BP recording on two consecutive follow-up visits (post-randomization) satisfied both the criteria of: (a) reduction of SBP at least 20 mm Hg and SBP <160 mm Hg and (b) DBP reduction at least 10 mm Hg and DBP <90 mm Hg from the BP level at randomization. We chose to use the ANBP2 study BP goal for defining 'target BP' in this paper rather than the current recommended clinical guideline of $<140/90$ mm Hg, as the participating GPs may have focused primarily on reaching the initial study goal. In addition to this, we have also reported on the contemporary guideline definition of BP $<140/90$ mm Hg achievement.

Statistical analysis

Descriptive statistics were used to summarize participant baseline demographic factors (for example, gender, age, education level and marital status) and clinical factors (for example, clinical measures and lifestyle-related factors; see Table 1). All values are expressed as mean ± s.d. unless otherwise specified. Residential location (postcode) was categorized using the Australian Standard Geographic Classification Remoteness Structure based on the concept that remoteness is an important factor in health service accessibility.[17] We also used the Socioeconomic Indexes for Areas to categorize the patient residence by postcode into an index of socioeconomic disadvantage considering its importance in health-care outcome.[18] In addition to baseline factors, we also used a number of in-study factors such as treatment regimen, number of BP-lowering drug used, GPs gender and change of GP to assess their associations with target BP achievement.

Analysis of variance techniques and unpaired Student's *t*-tests were used to assess gender differences for continuous variables. Chi-square tests were utilized to assess associations between dichotomous or categorical variables. Cox proportional hazards models were used to identify the factors associated with achieving 'target BP'. We censored the data when patients achieved target BP. If a patient achieved target BP then the first visit date of the two consecutive follow-up visits was taken as the censoring date whereas for those who did not achieve the target BP the last follow-up visit date (with BP recorded) was considered the censoring date.

The final multivariate Cox proportional model was adjusted for both demographic and clinical factors, which showed association ($P<0.10$) with target BP achievement on univariate analysis and also for patient's GP (cluster effect). Furthermore, a subgroup analysis was performed to explore the association of self-reported treatment adherence with target BP achievement, as adherence data were available for only two-thirds of the patients ($n=4039$). Treatment adherence information was collected once through a postal questionnaire survey using Morisky instrument, which is based on the following four-item scale (yes/no); (1) Do you ever forget to take your medicine? (2) Are you careless at times about taking your medicine? (3) When you feel better do you sometimes stop taking your medicine? (4) Sometimes if you feel worse when you take the medicine, do you stop taking it?; in September and October 2000.[19] Statistical analysis was performed using Stata version 11.2 for Windows (StataCorp LP, College Station, TX, USA).

RESULTS

A total of 6083 patients were randomized into the study of whom 99% ($n=6010$) had completed at least two follow-up visits at which BP was recorded. We considered these 6010 patients in the current analysis. These patients had a median of nine follow-up visits (interquartile range: 7–11; range 2–20 visits). The mean duration between the visits were 6 months (median 5.5 months).

Patient characteristics

Demographic and clinical characteristics of patients are summarized in Table 1. The baseline characteristics by-randomization was presented earlier.[16] Fifty-one percent of the study participants were female and the mean age was 72 ± 5 (s.d.) years. Mean ($\pm$ s.d.) SBP and DBP at the time of randomization were 168 ± 13 and 91 ± 8 mm Hg, respectively. Females had higher SBP and lower DBP compared with the males (Table 1). Both mean SBP and DBP as well as pulse pressure at the time of randomization differed by age group (Supplementary Table S1). Pulse pressure increased with advancing age, as, corresponding mean SBP increased and mean DBP decreased.

At randomization, an equal number of patients was randomized to ACE-I and diuretic based treatment group. However, in both treatment groups 83% of patients began to receive the randomized treatment following randomization, and at the end of the study 58% and 62% patients continued to receive the assigned ACE-I and diuretic treatment, respectively.[16] In following randomization to initial ACE-I or diuretic therapy, $>30\%$ (2029/6010, males 32% and females 35%) were prescribed additional BP-lowering medication. Most of the GPs managing the participants in the study were male (77%) and during the follow-up period 15% (922/6010) of the patients changed their GP. The change was highest in outer regional areas (25%) followed by major cities (16%) and inner regional areas (10%).

Treatment adherence information ($n=4039$) following randomization showed an adherence level of 67%.[20] Treatment adherence did not differ by patient gender, geographical location, index of socioeconomic disadvantage and randomized treatment group (data not shown).

On-treatment change in BP and pulse pressure

The mean ($\pm$ s.d.) achieved on-treatment SBP and DBP were 142 ± 16 and 78 ± 9 mm Hg respectively at the close of the study. The mean ($\pm$ s.d.) reduction in BP following randomization was SBP 26 ± 19 mm Hg and DBP 11 ± 10 mm Hg. Pulse pressure reduced on average 14 ± 16 mm Hg. On-treatment changes in BP and pulse pressure from randomization for different baseline and in-study variables are summarized in Supplementary Table S1. A significant difference in BP reduction (SBP/DBP, 22/11 mm Hg vs 27/13 mm Hg, $P<0.001$) was observed between those who did or did not have a change of doctor, although pulse pressure reduction (12 vs 14 mm Hg, $P=0.550$) was not significant (the *P*-values are adjusted for age, sex, baseline BP and treatment regimen). Differences in SBP and DBP reduction were observed by patients' educational level and doctors' gender (Supplementary Table S1).

The mean BP fall as well as pulse pressure reduction was greater among patients with higher SBP at the time of randomization

Table 1. Baseline demographic and clinical characteristics of the study participants

Variable	*Total* N = *6010*		*Male* N = *2930*	*Female* N = *3080*	P-*value*
	n	%	%	%	
Demographic factors:					
Age (years)					
Mean ± s.d.	71.9 ± 4.9 years		71.4 ± 4.8 years	72.4 ± 5.0 years	<0.001
65–69 years	2249	37.4	41.5	33.5	<0.001
70–74 years	1939	32.3	32.1	32.4	
75–79 years	1287	21.4	18.9	23.8	
80–84 years	535	8.9	7.4	10.3	
Education					
Primary school	1376	23.0	23.0	23.1	<0.001
Some secondary school	2610	43.7	41.1	46.1	
Completed secondary school or more	1988	33.3	35.9	30.8	
Marital status					
Currently married	3782	62.9	75.7	50.8	<0.001
Widowed	1515	25.2	12.2	37.6	
Separated or divorced	363	6.0	6.3	5.8	
Never married	302	5.0	5.0	5.0	
Defacto relationship	39	0.7	0.8	0.5	
Unknown	9	0.2	0	0.3	
Area of remoteness Australia					
Major cities	4966	82.6	81.4	83.8	0.005
Inner regional	751	12.5	12.8	12.2	
Outer regional	293	4.9	5.8	4.0	
Socioeconomic disadvantage index					
Highest	1573	26.2	28.3	24.3	0.001
2	1636	27.3	27.6	26.9	
3	1908	31.8	30.4	33.2	
Lowest	882	14.7	13.7	15.6	
Clinical factors:					
BMI, kg/m^2					
Mean ± s.d.	27 ± 4		27.2 ± 4	27.0 ± 5	0.0391
<25	1875	31.2	27.0	35.2	<0.001
25–<30	2827	47.1	52.9	41.5	
⩾30 (Obese)	1306	21.7	20.1	23.3	
Waist circumference, cm					
Mean ± s.d.		94.8 ± 12	100.4 ± 10	89.4 ± 11	<0.001
BP					
Systolic (mean ± s.d.)		168 ± 13	167 ± 13	169 ± 13	<0.001
Diastolic (mean ± s.d.)		91 ± 8	92 ± 8	90 ± 8	<0.001
Pulse pressure					
1 (31–66 mm Hg)	1516	25.2	30.1	20.5	<0.001
2 (67–77 mm Hg)	1594	26.5	28.0	25.1	
3 (78–87 mm Hg)	1514	25.2	23.7	26.6	
4 (88–137 mm Hg)	531	23.1	18.1	27.8	
Previously treated with BP-lowering drugs	3744	62.3	59.8	64.7	<0.001
Medical conditions					
History of diabetes	436	7.3	8.5	6.1	0.001
Previous coronary heart disease[a]	473	7.9	10.0	5.8	<0.001
Previous cerebrovascular disease[b]	275	4.6	5.4	3.8	0.005
Laboratory values					
Increased plasma creatinine (M >120 μmol/l; F >110 μmol/l)	715	11.9	15.8	8.2	<0.001
Raised total cholesterol (>6.5 mmol/l)	1282	22.2	13.7	30.3	<0.001
Low HDL (<1 mmol/l)	746	13.2	21.6	5.3	<0.001

Table 1. (Continued)

Variable	*Total* N = *6010*		*Male* N = *2930*	*Female* N = *3080*	P-*value*
	n	%	%	%	
Physical activity (in 2 weeks prior randomization)					
No exercise	1956	32.5	29.9	35.1	<0.001
1–6 hour exercise	1740	29.0	26.5	31.3	
⩾7 hour	2314	38.5	43.6	33.6	
Others					
Current smokers	423	7.0	8.5	5.7	<0.001
Current drinkers	4409	73.4	82.5	64.7	<0.001

Abbreviations: BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein. [a]Coronary heart disease included myocardial infarction, angina, coronary–artery bypass grafting, and percutaneous transluminal coronary angioplasty. [b]Cerebrovascular disease included stroke and transient ischemic attack.

(Supplementary Table S1). The mean SBP reduction was 39 ± 19 mm Hg among the highest quartile of SBP at randomization and 17 ± 16 mm Hg in lowest SBP quartile. Participants with previous history of BP-lowering medication had a greater BP reduction during the study than those who did not; however, no difference was observed in pulse pressure reduction. There was no difference in mean BP and pulse pressure reduction from randomization depending on patients' treatment based on either ACE-I or diuretics. Both the SBP and DBP, and pulse pressure reductions were higher among participants who were prescribed more than one BP-lowering drug. Among other baseline clinical characteristics, participants with previous history of coronary heart disease and antihypertensive therapy had greater BP (SBP/DBP) reduction than participants without this characteristic (Supplementary Table S1).

Target BP achievement and its association with baseline and in-study demographic and clinical characteristics

At the time of randomization, only 36% of the participants had a DBP below 90 mm Hg and none had a SBP below 160 mm Hg. During the study, target SBP was achieved in 61% and the DBP target was achieved in 59% with only 50% attaining both SBP and DBP targets once. Of the participants, 15% achieved the target BP on their first visit (median sixth visit). Figure 1 shows the proportion of participants who achieved target BP during the duration of the study following randomization. Ten percent of the participants achieved target BP within 6 months post-randomization. The ANBP2 trial BP goal of (SBP/DBP) <160/90 and at least 20/10 mm Hg of reduction was achieved once in at least 79% of the patient. Whereas an average BP of <140/90 mm Hg was achieved in only 36% of the patients after 4 years of randomization (DBP <90 mm Hg was achieved in 87% and SBP <140 mm Hg was achieved in only 37% patients).

Univariate analysis of demographic and clinical factors (data not shown) revealed that males, patients who were living in inner regional areas (compared with major cities), had increased plasma creatinine concentration, a wider pulse pressure, had previous history of antihypertensive therapy, and were using a combination of two or more BP-lowering drugs had strong positive association with achieving the target BP. On the other hand, participants who were aged >80 years, widowed, changed GP during the follow-up period and using ACE-I (compared with diuretics) were less likely to achieve the target BP. There was no association of BMI, previous history of cardiovascular event, smoking and alcohol consumption with achieving the BP target.

Multivariate analysis demonstrated that sex being male, living in inner regional areas of Australia (compared with living in major cities), having previous history of taking BP-lowering medication, having increased plasma creatinine concentration, and receiving a combination two or more BP-lowering drugs had the strongest association with achieving target BP (Figure 2). In contrast, seeking care from multiple GPs or changing GP, wider pulse pressure at randomization and advancing age were associated with increased rates of failure to achieve target BP. The association of failure to achieve target BP varied with age (interaction $P = 0.03$), with the strongest relations in the eldest (⩾80 years).

The achievement of target BP was not dependent on medication adherence in univariate analysis of the 4039 participants who completed and returned an adherence questionnaire during the study.

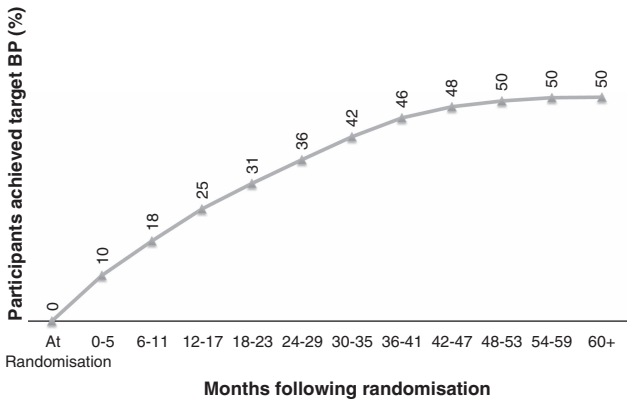

Figure 1. Proportion of participants achieved target BP following randomization in the ANBP2 study. A full colour version of this figure is available at the *Journal of Human Hypertension* journal online.

DISCUSSION

We have identified a number of factors both demographic and clinical associated with achieving a target BP in elderly hypertensive participants (age ⩾65 years) taking BP-lowering drugs. Overall, only 50% of the participants who were taking BP-lowering drugs following randomization achieved the BP target for both SBP and DBP, whereas 61% and 59% of the participants achieved target SBP and DBP, respectively. The proportion achieving the target SBP was similar to those reported in the Systolic Hypertension in the Elderly Program (SHEP) and European

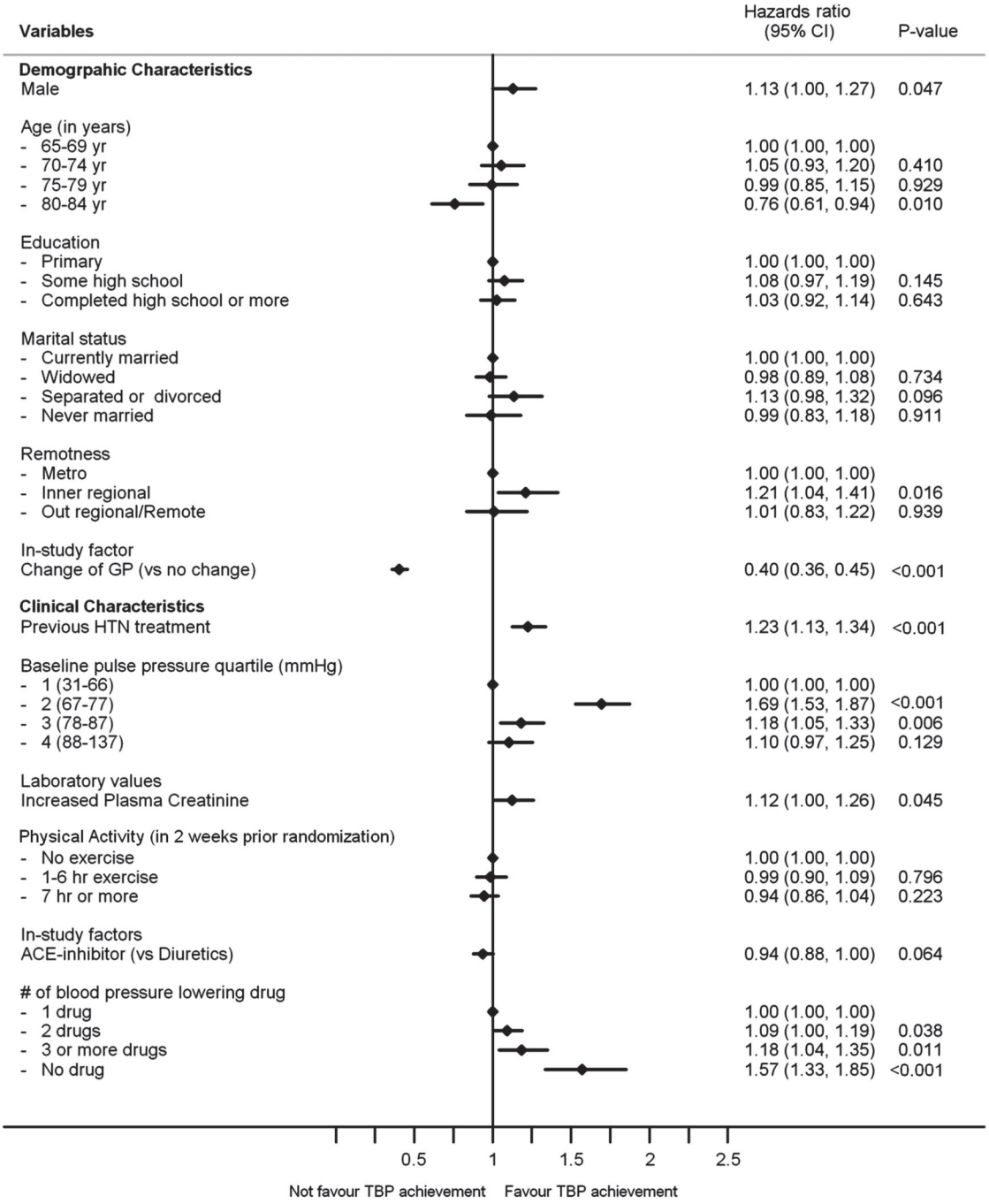

Figure 2. Association of baseline and in-study factors with achieving BP target (TBP) in ANBP2 study participants.

trial of isolated systolic hypertension (Syst-EUR), which had similar target BP.[21,22] However, the actual ANBP2 goal (SBP/DBP $<$160/90 mm Hg and at least 20/10 mm Hg reduction) achievement at least once was higher ($\sim$80%) than SHEP and Syst-EUR target SBP achievement. This degree of BP lowering in both SHEP and Syst-EUR was associated with significantly improved outcome.

The achievement of BP being $<$140/90 mm Hg according to the current BP management guideline was only in 36% of ANBP2 patients. This proportion is relatively lower than the observed rate of 66% and 67% among the participants of the Anti-Hypertensive and Lipid-Lowering Treatment to Prevent Heart Attack (ALLHAT) trial and the Controlled Onset Verapamil Investigation of Cardiovascular Endpoints (CONVINCE) trial, respectively.[15,23] There are several factors such as free medications, enhanced definite access to care, focused motivated physicians and 'goal-oriented' BP management, as well as not stopping BP-lowering drugs before randomization that may account for the higher rates of control in these randomized clinical trials (in ALLHAT and CONVINCE trial 27% and 20% of patients had both SBP/DBP $<$140/90 mm Hg at baseline), which were not replicated in routine clinical practice as seen in the ANBP2. Another reason may well be that once the trial goal was achieved in the ANBP2, GPs were not actively trying to lower BP levels further to the more contemporary goal of $<$140/90 mm Hg in this elderly hypertensive population. Advanced age is also strongly related to uncontrolled hypertension as well as elevated SBP.[24] Our

findings also shows advanced age is related to less target BP achievement.

We observed that the extent of BP reduction (especially for DBP) was greater, and attainment of BP targets was more frequent, among males. It is possible that this could indicate the greater arterial stiffness of older females, which in turn may cause augmentation of SBP and pulse pressure because of earlier pulse wave reflection.[25,26] The finding of better target BP achievement in males is also consistent with studies conducted in both a US population and in a Belgian cohort,[15,24,27–29] but contradicts earlier findings in a French population.[30,31] Several other factors such as awareness and risk perception about absolute cardiovascular disease risk of high BP in male and females, and participants' and physicians' treatment preference have also been previously reported to have an impact on achieving BP targets.[31,32]

Our findings show that the ability to achieve the BP targets differed by place of residence in Australia with those living in inner regional areas being more likely to achieve target BP than those living in major cities or outer regional areas. In outer regional areas, this may be due to a limited access to health care as there are relatively fewer GPs in these areas.[33] In metropolitan areas, it may be due to change of GPs, which is more common in outer regional and major cities compared with inner regional areas. The change of GPs during the follow-up period was strongly inversely associated with the in-study target BP achievement. However, the study did not collect information on the reasons for changing GPs and participants' satisfaction level; therefore, we do not know if the GPs in particular regions changed frequently or if the participants actively changed their GPs because of some other reason.

Clinical factors such as previous history of BP-lowering medication and raised plasma creatinine were associated with more likely achievement of target BP. These findings, however, contradict earlier findings from ALLHAT study.[15] Possible explanation may relate to differences in study design, for example, ANBP2 participants were completely withdrawn from previous medication before study entry, whereas ALLHAT participants were switched from existing treatment to nominated treatment. The other possible reasons for these findings in ANBP2 are that the GPs may have already identified those previously treated as having a greater overall risk and in addition the presence of comorbidities may have influenced the perception of individual absolute risk and thus the intensity of treatment. As reflected in BP management guidelines,[1,6,7] major outcome trials of BP lowering have shown that combinations of BP-lowering drugs will improve BP control across the population, including the elderly. In our study, about 34% of the participants received two or more BP-lowering drugs and participants receiving more than one BP-lowering drug had better target BP achievement. Our findings thus concur with those in other major outcome trials and support the recommendation to use combinations of BP-lowering drugs particularly those with different mechanisms of action.

Participants' adherence to therapy has an important role in BP control and clinical outcomes.[20,34,35] However, in this study the subgroup analyses did not show any significant difference in attaining BP targets achievement according to adherence to therapy. The level of patient adherence is usually difficult to measure by self-assessment and this may explain our failure to demonstrate a relationship between medication adherence and achievement of target BP.

There are a number of limitations related to the present findings. First, BPs were measured by the GPs or nurses with sphygmomanometers in their own GP clinics. Measured BP can vary by operator and also by type of machine. To minimize risk of such measurement error a standard procedure was developed and training was provided to GPs and nurses for measuring BP. Second, we do not have information on the regularity with which these sphygmomanometers were calibrated. If not regularly calibrated, variations in BP readings may take place. Third, dosing of BP-lowering medication, which could produce substantial differences in BP control rates was not considered in the analysis. In ANBP2, the GPs were allowed to increase the drug dose and/or include additional BP-lowering drug to achieve target BP. The study was conducted in Australia and therefore the findings may not be applicable in countries with a different health system, GDP or demographic profile. However, ANBP2 was a pragmatic 'real world' study and the factors identified will be at play when treating physicians make treatment decisions on a day to day basis.

Despite these limitations, the results of our large prospective study are likely to be valid and are generalizable in similar contexts. Our participants were recruited from GP clinics and managed by their GPs as part of their regular practice. The long follow-up period and the relatively high average number of visits at which BP was measured should have ensured that the participants had a good chance of achieving target BP and then maintaining it over a relatively long period of observation. Our findings identify the difficulties in achieving target BP in elderly hypertensive patients. Continuity of care may be a key service factor for individuals to achieve target BP's on-treatment.

In conclusion, we identified several factors related to the achievement of target BP in elderly hypertensive patients receiving BP-lowering medications. Given the escalating burden of hypertension, strategies directed at mitigating these factors need to be further developed and refined. Such strategies should include targeted education of the elderly population to increase awareness of BP and its risk especially among women and those who are living in major cities/outer regional areas, particularly in relation to maintaining a consistent relationship with one treating GP wherever possible. Designing future interventions to achieve the target BP should take the demographic and clinical characteristics of the target population into account for improved outcome.

What is known about this topic

- Achieving the guideline recommended target BP in the elderly is difficult.
- To achieve BP control, more than one antihypertensive drug is often required.
- Factors associated with achieving BP control in the elderly are not clearly recognized and are controversial across different contexts.

What this study adds

- Demographic factors in addition to clinical factors are important determinants of achieving BP control.
- Continuity in primary care may be an important demographic factor associated with achieving BP control in the elderly.
- Treatment based on either ACEI or diuretics does not influence the attainment of BP targets in elderly hypertensive when adjusted for other demographic and clinical factors.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

ANBP2 was supported by the Australian Commonwealth Department of Health and Aging; the National Health and Medical Research Council of Australia (grant 546272); and Merck Sharp & Dohme, Australia. CMR is supported by a senior research fellowship from NHMRC. We are indebted to the participants, study staff, data management centers and ANBP2 management committee. The management committee consists of the following members: LMH Wing (Chair), CM Reid, LJ Beilin, MA Brown, GLR Jennings, CI Johnston, JJ McNeil, JE Marley, TO Morgan, P Ryan, J Shaw (deceased), MJ West and G MacDonald.

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