

ambulatory equivalents were another 3-4 mm Hg lower (daytime -9/-6 for 140/90 mm Hg and -5/-4 for 130/80 mm Hg) (see supplementary table S2).

Ambulatory equivalents for seated clinic blood pressure measured by doctor

In a separate analysis, we compared 1593 doctor measured clinic blood pressure values with ambulatory blood pressure by least product regression to determine whether ambulatory thresholds differed from those calculated using values measured by trained staff. The regression degree of correlation was somewhat lower in this group than in the larger group, with r values ranging from 0.41 to 0.54 (supplementary figure S1). While slopes and intercepts differed from 1 and zero respectively, indicating similar fixed and proportional bias to the main study, the least product regression lines followed the major axis of the data ellipsoid. The daytime systolic/diastolic ambulatory blood pressure indicating the minimum for grade 1 hypertension was estimated to be 11/9 mm Hg lower than the equivalent clinic value (table 2); for target blood pressure in patients with one condition the equivalent was 7/7 mm Hg lower, and for the upper limit of normal blood pressure the equivalent was 3/10 mm Hg lower. In men and women the ambulatory equivalents for daytime diastolic pressure were not affected by age, but those for systolic pressure were lower in older people than in younger ones (table 3).

Comparison between ambulatory equivalents for PAMELA study and Australian data

Although the study populations differed in that clinic and ambulatory blood pressure were lower for the PAMELA study than for the Australian data, even after adjustment for age, sex, and treatment status, the daytime ambulatory blood pressure equivalents for doctor measured clinic blood pressure of 140/90 mm Hg in PAMELA were almost identical to those in the present study (within 1 mm Hg; table 4). Limiting the Australian participants to match those of the PAMELA study by age, sex, and treatment status did not alter this value. Furthermore, the daytime ambulatory blood pressure equivalents for trained staff measured clinic

blood pressure of 140/90 were 8/5 mm Hg higher than those of the PAMELA study and again were not affected by limiting the participants to match the criteria of the PAMELA study (10/5 mm Hg) (table 4).

Comparison between clinic sitting and reclining blood pressure

To determine whether reclining clinic measurements could also be substituted for seated equivalents, we examined the relation between these two measurements in a subgroup of 1267 participants. There was a very high correlation between clinic blood pressure measured sitting and reclining ($r=0.85$ for systolic blood pressure and 0.81 for diastolic blood pressure). Diastolic blood pressures were effectively the same in either position since the slope and intercept 95% CIs overlapped with 1 and 0, respectively. Systolic blood pressures were slightly higher in the reclining than in the sitting position, but only at higher systolic blood pressure values (3 mm Hg higher at 120 mm Hg and 5 mm Hg higher at 160 mm Hg, paired t test, $P<0.0001$, $t=14$).

DISCUSSION

We used least product regression to provide ambulatory blood pressure equivalents for the definition of hypertension and its severity and for common treatment targets based on seated clinic measurements. When measurements were taken by trained staff, the daytime ambulatory blood pressure equivalents for the lower limit of grade 1 hypertension (140/90 mm Hg) were 4/3 mm Hg lower than the clinic values. For the target clinic value in patients with one associated clinical condition (130/80 mm Hg) the daytime ambulatory blood pressure equivalent was 2/2 mm Hg lower, and for patients with significant proteinuria who require a target clinic blood pressure of 125/75 mm Hg, the daytime ambulatory equivalent was 1/1 mm Hg lower. Thus our analysis shows that the closer the patient's blood pressure is to normal levels, the closer is the agreement between daytime ambulatory and clinic blood pressure. On the other hand, the higher the blood pressure, the greater the difference between ambulatory and clinic blood pressure.

Table 3 | Daytime systolic/diastolic ambulatory blood pressures by age and sex predicted from seated clinic blood pressure levels measured by staff; values in mm Hg

	Clinic seated blood pressure	Combined (n=5327)			Men			Women		
		24-hour	Night	Day	25-44 (n=468)	45-64 (n=1057)	≥65 (n=800)	25-44 (n=616)	45-64 (n=1112)	≥65 (n=1094)
Grade 3 hypertension	>180/110	163/101	157/93	168/105	176/104	170/105	167/104	171/105	167/103	164/102
Grade 2 hypertension	>160/100	148/93	139/84	152/96	158/96	154/96	151/96	154/96	151/95	149/93
Grade 1 hypertension	>140/90	133/84	121/76	136/87	140/87	138/88	136/87	137/87	135/86	133/85
Target blood pressure plus one condition	<130/80	125/76	112/67	128/78	131/79	130/79	128/79	129/78	126/77	125/77
Target blood pressure with proteinuria	<125/75	121/71	107/63	124/74	127/75	126/75	125/75	124/73	122/73	121/72
Normal blood pressure	<120/80	117/76	102/67	120/78	122/79	122/79	121/79	120/78	118/77	118/77

Table 4 | Predicted systolic/diastolic ambulatory blood pressure from PAMELA study and the present study measured by physician or staff, with and without age and treatment restrictions. Blood pressure values in mm Hg.

	PAMELA (n=1438)	Present study: doctor measured		Present study: staff measured	
		Combined seated (n=1490)	Combined seated (age, sex, treatment adjusted) (n=112)	Combined seated (n=5327)	Combined seated (age, sex, treatment adjusted) (n=1027)
Female sex	50.8%	833 (55.9%)	58 (50.9%)	2888 (54.2%)	522 (50.9%)
Treated individuals excluded	Yes	No	Yes	No	Yes
Mean age in years (SD)	46.4 (11.9)	53.6 (15.8)	42.1 (10.7)	57.2 (15.9)	46.3 (10.2)
Age range	25-64	15-94	25-64	18-98	25-64
Clinic blood pressure	128/82	150/89	146/91	142/82	137/87
Absolute ambulatory blood pressure					
24 hour	118/74	132/77	127/80	134/77	132/82
Daytime	123/79	136/80	132/83	137/80	136/85
Night time	108/64	121/68	113/68	122/68	117/71
Predicted ambulatory blood pressure for grade 1 hypertension (clinic blood pressure 140/90)					
24 hour	123/77	126/78	123/78	133/84	134/85
Daytime	128/82	129/81	128/82	136/87	138/88
Daytime difference between PAMELA and present study		1/-1	-1/-1	8/5	10/5
Night time	112/67	113/69	109/66	121/76	119/74

Comparison with other studies

Previous studies have mainly concentrated on defining the upper limit of normal for ambulatory blood pressure and have not extended the analysis to predictions for grade 2 (moderate) or grade 3 (severe) hypertension or to lower blood pressure targets adjusted for comorbidities such as diabetes and renal disease. Consensus papers from an ad hoc committee of the American Society of Hypertension²⁶ and from the National Heart Foundation of Australia¹¹ have concluded that the daytime ambulatory blood pressure equivalent for the lower limit of grade 1 hypertension (140/90) is 135/85 mm Hg, which is similar to but slightly less than the equivalent values of 136/87 mm Hg determined in the present study.

The consensus papers have been mainly based on large, multicentre randomised population studies involving measurements from people considered normotensive¹² and from the PAMELA study of normotensive people from Monza, Italy.¹⁵ The latter study predicted somewhat lower ambulatory blood pressure equivalents than our study (for clinic 140/90 mm Hg, equivalents of 128/82 mm Hg for daytime and 125/80 mm Hg for 24 hour). Nevertheless, when we limited our data set to the same age range, excluded treated participants, and adjusted the male to female ratio to be identical to that of the PAMELA cohort, these changes made little difference to the predicted values.

The main difference seems to arise from the fact that in the PAMELA study clinic blood pressure was measured by doctors, since the differences between studies was almost eliminated when we used only the blood pressure values measured by doctors. Therefore the most likely reason for our study showing greater equivalence between clinic and daytime ambulatory blood pressure is that we have reduced the “white coat” effect by using clinic blood pressures measured by trained staff. Our finding that blood pressure

recorded by doctors was higher by 9/7 mm Hg than that recorded by other health professionals is in accord with previous studies that compared nurse and doctor measured blood pressure.²⁷ A large study by La Batide-Alanore and colleagues showed that nurses recorded 6/8 mm Hg lower blood pressure than doctors.²⁸ This finding led to the suggestion that routine management of the hypertensive patient should not rely solely on the doctor’s assessment of blood pressure.²⁸ Their finding that the nurse recorded blood pressure was closer to the patient’s daytime average ambulatory blood pressure than the pressure recorded by the doctor also closely concurs with the current study.

One of the major differences between the population samples from our present study and previous reports is that we included a higher proportion of patients given antihypertensive medication who were referred for assessment of the effectiveness of treatment.^{13 16 17} Little difference was observed in the predicted values when treated participants were excluded, suggesting that treatment does not significantly affect the relation between clinic and ambulatory blood pressure measurements per se. These adjustments also included a slight change in the male to female ratio and age range but this does not indicate that age and sex were not important in the calculations of ambulatory blood pressure equivalents. Estimates were 2-3 mm Hg lower for women than men for systolic and diastolic blood pressure and lower in older participants of both sexes, but only for systolic blood pressure. Thus more accurate ambulatory blood pressure treatment targets may be attained by taking age and sex into consideration.

Strengths and limitations of study

A strength of the present study is that analyses were based on patients for whom treatment equivalents are

WHAT IS ALREADY KNOWN ON THIS TOPIC

Ambulatory blood pressure predicts cardiovascular outcome better than clinic blood pressure, with known equivalent thresholds for diagnosis of mild hypertension

Guidelines for management of hypertension in patients with pre-existing cardiovascular disease or risk factors suggest that target values should be different from those in patients without such factors, but ambulatory equivalents have not been defined

Blood pressure measured in the clinic by doctors tends to be higher than that measured by nurses

WHAT THIS STUDY ADDS

Regression analysis showed that the hypertension thresholds and target values for daytime ambulatory blood pressure were slightly lower than the equivalent clinic values

Ambulatory values were 1/2 mm Hg lower for women than for men and 3/1 mm Hg lower in older people (≥ 65 years) than in younger people

Because doctors' measurements of clinic blood pressure were higher than those of trained staff, they are inappropriate for estimation of ambulatory blood pressure treatment thresholds

most relevant—that is, with suspected or treated hypertension—from 11 different hypertension clinics across all Australian states. Furthermore we also showed marked differences in the estimates depending on whether the clinic blood pressure was measured by a doctor or a trained staff member. Another strength of the current study was the use of the least product method for regression estimates, which provides a statistically appropriate method for calculating ambulatory blood pressure monitoring equivalence, particularly in cases where there is systematic and proportional bias (making the least squares method inappropriate).²⁹ This can be clearly appreciated by inspection of the regression lines and data distribution where the least product method, but not the least squares method, followed the major axis of the ellipsoid.

A possible limitation of our study is that we have used the larger population (with and without comorbidities) in the regression analysis to predict target values for each, respectively. Thus a further future refinement would be to document and adjust for comorbidities and to determine whether this makes a significant difference in the predictive values.

Conclusions and policy implications

In conclusion, the present study provides a range of daytime ambulatory blood pressure measurements equivalent to recognised diagnostic thresholds and target clinic blood pressure. These values are only slightly below clinic values measured by trained staff and can be used to guide the management of hypertension. It also provides separate ambulatory blood pressure targets for men and women at different ages. The benefits of this study are that we used blood pressure measurements from both treated and untreated individuals, a population that is representative of clinical practice. Current hypertension guidelines propose operational thresholds for normality. We now suggest that the

guidelines can include the thresholds identified in the current study to guide management of hypertension.

This research is part of a joint initiative between the High Blood Pressure Research Council of Australia and the National Heart Foundation of Australia, which aims to support appropriate use and interpretation of ambulatory blood pressure monitoring and effective management of blood pressure in the primary care setting.

Contributors: GAH was involved in study conception and design, study supervision, statistical analysis, preparation of graphs and tables, data interpretation, and drafting, revision, and finalising of the paper. ASM and KAD were involved in study conception and design, study supervision, data interpretation and drafting, revision, and finalising of the paper. NB, MAB, DC, PRCH, JH, AAM, BPM, MRN, and JES and were involved in study supervision, data interpretation, and revision and finalising of the paper. LJB, AJB, MS, and JPC and were involved in data interpretation and revision and finalising of the paper. JL was the study statistician and was involved in data analysis, drafting and revision of the paper. GAH is the guarantor. All authors had full access to all the data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. We thank Kanella Chatzivlastou, Melinda Carrington, Carla M. Morley, Kim N Do, Karen Hall, Mark J Penny, Lai H Siew, and Agnes Ross for contributions to collection and analysis of data.

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Data sharing: no additional data available.

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