

# The value of ambulatory blood pressure in older adults: the Dublin outcome study

MARIAN L. BURR<sup>1</sup>, EAMON DOLAN<sup>1</sup>, EOIN W. O'BRIEN<sup>1</sup>, EOIN T. O'BRIEN<sup>2</sup>, PATRICIA MCCORMACK<sup>3</sup>

<sup>1</sup> The Lewin Stroke and Rehabilitation Unit, Cambridge University Hospitals NHS Foundation Trust, Addenbrooke's Hospital, Hills Road, Cambridge, UK

<sup>2</sup> The Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Belfield, Dublin 4, Ireland

<sup>3</sup> Blood Pressure Unit, Beaumont Hospital, and Department of Clinical Pharmacology, Royal College of Surgeons in Ireland, Dublin, Ireland

Address correspondence to: Marian L. Burr. Email: marianlurr@doctors.org.uk

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## Abstract

**Background:** ambulatory blood pressure (ABPM) appears to be a more accurate predictor of cardiovascular outcome than blood pressure (BP) measured in the clinic setting in younger adults.

**Objectives:** the purpose of this study was to determine if ABPM predicted total and cardiovascular mortality independently of clinic BP and other cardiovascular risk factors in those aged 65 years and over.

**Methods:** one thousand one hundred and forty-four individuals aged 65 and over referred to a single BP clinic had 24-h ABP measurement and clinic measurement at baseline off treatment. There were 385 deaths (of which 246 were cardiovascular) during a mean follow-up period of 6.7 years.

**Results:** with adjustment for gender, age, risk indices and also for clinic BP, a higher mean value of ABPM was an independent predictor of cardiovascular mortality. The relative hazard ratio for each 10-mmHg rise in systolic blood pressure (SBP) was 1.10 (1.06–1.18,  $P < 0.001$ ) for daytime and 1.18 (1.11–1.25,  $P < 0.001$ ) for night-time SBP. The hazard ratios for each 5-mmHg rise in diastolic blood pressure (DBP) were 1.05 (1.00–1.10,  $P = \text{NS}$ ) for daytime and 1.09 (1.04–1.14,  $P < 0.001$ ) for night-time diastolic pressure. The hazard ratios for night-time ABPM remained significant after adjustment for daytime ABPM.

**Conclusions:** ambulatory measurement of BP is superior to clinic measurement in predicting cardiovascular mortality in elderly subjects. Night-time BP is the strongest predictor of outcome in this age group.

**Keywords:** hypertension, clinic blood pressure, ambulatory blood pressure, outcome, older, elderly

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## Introduction

Ambulatory blood pressure monitoring (ABPM) is being increasingly used in the assessment of hypertension in all age groups. There is a continuous relationship between blood pressure (BP) and cardiovascular risk amongst older people [1]. This is seen irrespective of the method of BP measurement used. However, a single ABPM recording provides multiple BP measurements over a 24-h period, thus providing a better estimate of the daily BP load than isolated clinic measurements. ABPM also allows identification of white-coat hypertension, which is more common in the elderly [2]. We have recently seen that the circadian pattern of BP is important in relation to cardiovascular risk in the elderly. This of course is only available to us through the use of 24-h ambulatory monitoring.

There is increasing evidence that ABPM is a more accurate predictor of cardiovascular morbidity and mortality than clinic blood pressure measurement (CBPM) [3–12]. In addition, evidence is accumulating that night-time BP is a better predictor of outcome than daytime BP [7, 10, 12–18]. However, only a few smaller studies have compared the prognostic value of ABPM and CBPM in elderly people and only one of these assessed the ability of ABPM to predict mortality [3, 4, 7].

In view of the lack of data regarding ABPM in older people, the objective of this study was to determine the additional value of ABPM over CBPM, and also night-time over daytime BP, in terms of predicting mortality in elderly hypertensive patients. We followed up 1,144 hypertensive patients aged 65 and over from a single centre for up to 20 years.

## Methods

### Study population

The BP unit (formerly located at the Charitable Infirmary and now based at Beaumont Hospital in Dublin) has been in operation for 22 years. The majority of patients are referred to the unit by their family doctors because of an elevated CBPM. Fourteen thousand, four hundred and fourteen such patients were entered into a database during the study period (1 June 1980 to 30 September 2002). To be eligible for the inclusion in the present report; patients had to be 65 years or older and either untreated at baseline or to have had all anti-hypertensive drugs discontinued for a week prior to their baseline visit to the unit. Demographic details and cardiovascular risk factors [sex, age, body mass index (BMI), smoking status, presence of diabetes mellitus and history of previous cardiovascular events] had to be recorded; and the ABPM record had to include at least 10 daytime and 5 night-time readings. The total number of participants fulfilling the entry criteria on 30 September 2002 was 1,144. The Hospital Ethics Committee approved the study.

### Clinic blood pressure measurement

A nurse measured BP in the non-dominant arm after 5 min of quiet sitting in accordance with contemporary recommendations [19] using either a standard mercury sphygmomanometer or a calibrated and validated automated sphygmomanometer—the Omron HEM-705CP [20]. CBPM was calculated as the mean of three measurements.

### Ambulatory blood pressure measurement

ABPM measurements were made every half-hour throughout the 24-h period using SpaceLabs 90202 and 90207 monitors (SpaceLabs Inc., Wokingham, Berkshire, UK), both of which have been previously shown to be accurate [21, 22]. All data were transferred into a software package (Dabl Cardiovascular, Dabl Limited, Dublin, Ireland) [23], which allows calculation of systolic blood pressure (SBP) and daytime blood pressure (DBP) for the daytime period (average of readings between 09:00 and 21:00 h, the night-time period (average of readings between 01:00 and 06:00 h) and the 24-h period without applying any editing criteria [24]. ABPM measurements were time weighted. Hypertension was defined as a mean daytime ABP of at least 135 mmHg systolic or 85 mmHg diastolic [25].

### Mortality outcome

Mortality outcome was ascertained by searching a national computerised register of deaths for each individual whose name appeared in the Dabl BP database. This process has been described previously [26]. This process provided definite evidence that 385 people from the 1,144 individuals in the study cohort had died by 30 September 2002. The death certificate of each individual was examined and the cause of death was coded according to the World Health

Organization's International Classification of Diseases, 9th Revision (ICD-9) [27]. Cardiac mortality included myocardial infarction (ICD-9, 4, 100 to 4,109), heart failure (4,280 to 4,289), sudden death (7,980 to 7,989) and chronic coronary heart disease (4,140 to 4,149). Cardiovascular mortality consisted of cardiac mortality, stroke (4,300 to 4,246) and other vascular deaths.

### Statistical analysis

The analyses were performed using SAS software, version 9 (SAS Institute Inc, Cary, NC). The baseline characteristics of those patients with fatal cardiovascular events and those without fatal events were compared using the large sample  $z$  test to compare means for continuous variables, and the  $\chi^2$ —statistic to compare proportions for categorical variables. To assess the independent effect of the different BP parameters, we introduced CBPM, daytime ABPM, night-time ABPM and 24-h ABPM as continuous variables in Cox proportional hazards regression. Relative hazard ratios and 95% confidence intervals were calculated for each 10- and 5-mmHg increase in SBP and DBP, respectively. To exclude the effects of potential confounding variables, adjustments were made for gender, age, BMI, presence of diabetes mellitus, history of cardiovascular events and current smoking status. We made a further adjustment for CBPM in order to ascertain the independent prognostic value of ABPM for mortality risk.

## Results

### Baseline characteristics

The characteristics of the patient populations are shown in Table 1. One thousand one hundred and forty-four patients were included in the study. Mean follow-up was 6.7 years. Mean age at baseline was 73.1 years (range from 65 to 92.4 years). There were 385 deaths, of which 246 were cardiovascular. The prevalence of known cardiovascular risk factors was higher among those patients who died of cardiovascular causes.

### Clinic and ambulatory blood pressures as predictors of mortality risk

Table 2 shows the relative hazard ratios for 10- and 5-mmHg increases in SBP and DBP, respectively, before and after adjustment for CBPM. With adjustments applied for baseline characteristics, the systolic ABPM predicted cardiovascular mortality outcomes over and above systolic CBPM ( $P < 0.001$ ). The hazard ratios associated with a 10-mmHg increase in SBP were 1.10 (95% CI 1.06–1.18;  $P < 0.001$ ), 1.18 (95% CI 1.11–1.25;  $P < 0.001$ ) and 1.17 (95% CI 1.09–1.26;  $P < 0.001$ ) for daytime, night-time and 24-h ABPM, respectively. The corresponding adjusted relative hazard ratios associated with a 5-mmHg increase in DBP were 1.05 (95% CI 1.00–1.10;  $P = \text{NS}$ ), 1.09 (95% CI 1.04–1.14;  $P < 0.001$ ) and 1.08 (95% CI 1.02–1.14;  $P < 0.01$ ). Figure 1 demonstrates the absolute 5-year cardiovascular risk, after

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**Table 1.** Characteristics of study population

	Alive	Dead (cardiovascular cause)
<i>n</i>	759	246
Age (years)	72.2 (11.2)	74.7 (8.9)*
Female (%)	54.8	43.5*
Body-mass index (kg/m <sup>2</sup> )	26.5 (3.6)	24.8 (3.4)
Current smoking (%)	22.9	30.6*
Diabetes (%)	7.2	11.1*
Previous cardiovascular complications (%)	9.3	23.1*
Clinic SBP	172.1 (26.8)	171.9 (31.1)
Clinic DBP	89.2 (14.6)	90.3 (16.1)
Daytime SBP	147.4 (18.4)	150.1 (22.8)*
Daytime DBP	89.1 (12.5)	88.2 (14.7)
Night-time SBP	133.2 (18.7)	141.4 (25.3)*
Night-time DBP	74.8 (12.8)	78.8 (15.2)*
24-h SBP	143.1 (20.3)	148.3 (25.1)*
24-h DBP	82.1 (11.2)	84.6 (13.1)*

Values are means (±SD) or number of subjects (%)

Body mass index is the weight in kilograms divided by the square of height in metres.

\* Statistical significance ( $P < 0.05$ ) of difference between the alive group and cardiovascular dead group.

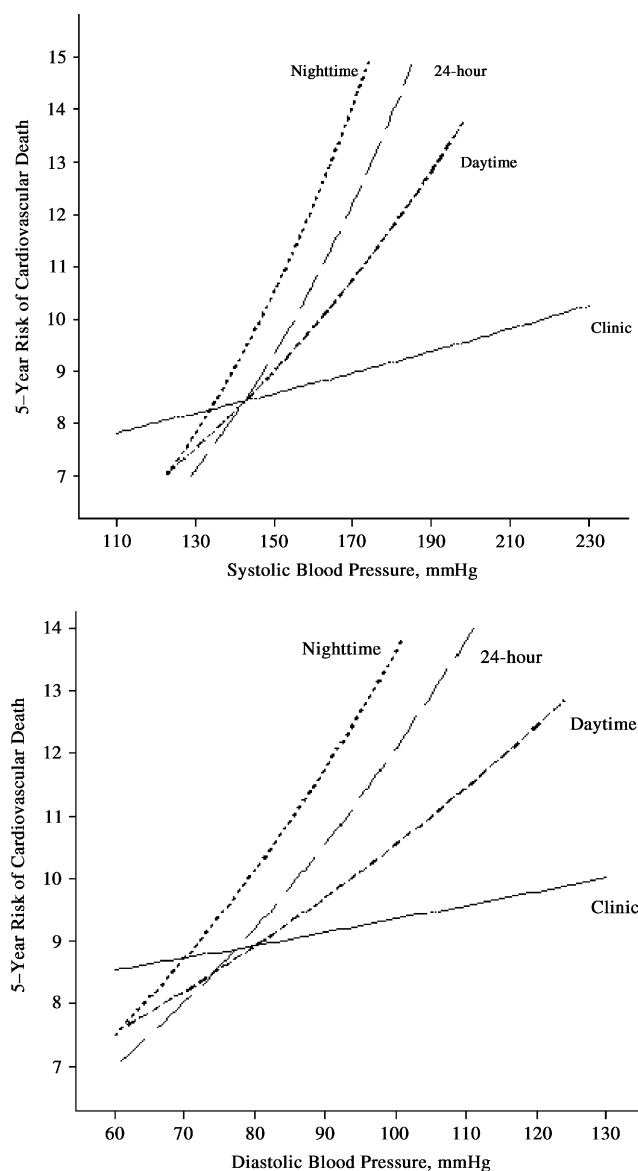
adjustment for other covariates, in relation to baseline ABPM and CBPM.

### Discussion

The results presented here demonstrate that ABPM is a more accurate predictor of cardiovascular mortality than CBPM in elderly hypertensive patients and that night-time BP is a better predictor than daytime. After adjusting for CBPM, for each 10-mmHg increase in daytime SBP and night-time SBP, the relative risk of cardiovascular death rose by 10% and 18% respectively. In contrast, for a 10-mmHg increase in clinic SBP there was no significant increase in mortality.

There is now convincing evidence that ABPM is a better predictor of cardiovascular risk than CBPM [3–12]. This was first demonstrated by Perloff *et al* in 1983 who followed up 1,076 hypertensive patients for a mean of 5 years and found that for any given value of clinic BP, a higher ABPM was associated with increased cardiovascular events [5]. Since then, several different studies have reproduced these findings and shown that ABPM predicts cardiovascular morbidity more accurately than CBPM in hypertensive patients [3, 4, 6–9]. More recently, the full report of the Dublin Outcome Study confirmed that ABPM also predicts cardiovascular mortality independently of CBPM [10]. Two large prospective population-based studies have extended these findings to normotensive as well as hypertensive individuals in Japanese and Western populations [11, 12]. In both these studies, on inclusion of ABPM and CBPM in the same multivariate models, ABPM significantly predicted mortality, whereas CBPM did not.

In contrast, the published evidence relating specifically to ABPM in the elderly is more limited. In a prospective



**Figure 1.** Adjusted 5-year risk of cardiovascular death in the study cohort of 1,144 older patients for CBPM and ABPM. Using multiple Cox regression, the relative risk was calculated with adjustment for baseline characteristics including gender, age, presence of diabetes mellitus, history of cardiovascular events and smoking status. Five-year risks are expressed as number of deaths per 100 subjects.

population-based study of 872 Swedish elderly men, higher ambulatory SBP and pulse pressure both predicted cardiovascular events. However, after adjustment for CBPM, only ambulatory pulse pressure and not SBP significantly predicted outcome [3]. In 2001, Khattar *et al* showed in a group of 142 elderly hypertensive subjects that intra-arterial ambulatory SBP predicted cardiovascular morbidity whereas clinic BP did not. However, the numbers were too small to show a significant association between ABPM and mortality [4]. The Systolic Hypertension in Europe (Syst-Eur) trial in

Table 2. Relative hazard ratios associated with CBPM and ABPM

		Unadjusted for clinic blood pressure				Adjusted for clinic blood pressure			
		All cause mortality	Cardio-vascular	Stroke	Cardiac	All cause mortality	Cardio-vascular	Stroke	Cardiac
Number of events		385	246	66	162	385	246	66	162
Systolic blood pressure	Clinic	0.99 (0.96–1.03)	1.02 (0.98–1.07)	1.03 (0.95–1.12)	1.02 (0.97–1.08)				
	Daytime	1.05 (1.00–1.10)	1.10 (1.03–1.17)**	1.12 (1.00–1.25)	1.10 (1.02–1.19)*	1.06 (1.01–1.13)*	1.10 (1.06–1.18)***	1.12 (0.99–1.27)	1.11 (1.02–1.21)*
	Night-time	1.11 (1.06–1.16)***	1.17 (1.11–1.24)***	1.24 (1.12–1.37)***	1.14 (1.07–1.23)***	1.13 (1.08–1.19)***	1.18 (1.11–1.25)***	1.24 (1.12–1.38)***	1.15 (1.07–1.24)**
	24-h	1.09 (1.03–1.15)**	1.15 (1.08–1.23)***	1.20 (1.07–1.35)**	1.15 (1.06–1.24)***	1.12 (1.06–1.19)***	1.17 (1.09–1.26)***	1.22 (1.07–1.40)**	1.16 (1.06–1.27)**
Diastolic blood pressure	Clinic	1.00 (0.97–1.04)	1.01 (0.97–1.05)	1.05 (0.98–1.13)	0.98 (0.94–1.04)				
	Daytime	1.04 (1.00–1.08)	1.05 (1.00–1.10)	1.11 (1.02–1.21)*	1.02 (0.96–1.08)	1.04 (1.00–1.08)	1.05 (1.00–1.10)	1.10 (1.00–1.20)	1.02 (0.96–1.09)
	Night-time	1.08 (1.04–1.12)**	1.08 (1.04–1.13)***	1.15 (1.06–1.25)**	1.05 (1.01–1.11)*	1.09 (1.05–1.13)***	1.09 (1.04–1.14)***	1.14 (1.05–1.25)***	1.06 (1.00–1.12)
	24-h	1.07 (1.03–1.11)**	1.08 (1.02–1.13)**	1.16 (1.06–1.27)**	1.05 (1.00–1.10)	1.08 (1.03–1.13)***	1.08 (1.02–1.14)**	1.15 (1.04–1.27)*	1.05 (0.98–1.13)

Relative hazard rates (95% confidence intervals) for each 10-mmHg increase in systolic pressure and 5-mmHg increase in diastolic pressure with adjustments applied for baseline characteristics including gender, age, body mass index, presence of diabetes mellitus, history of cardiovascular events and smoking status along with further adjustment for CBPM. Cardiac fatal endpoint includes heart failure, myocardial infarction and sudden death. Significance of the hazard ratios \*  $P < 0.05$ , \*\*  $P < 0.01$ , \*\*\*  $P < 0.001$

1999 followed up 808 patients over 60 years with isolated systolic hypertension for a mean of 4.4 years. Separate analysis of the 393 patients in the placebo (untreated) group showed that, after adjustment for CBPM, ambulatory daytime, night-time and 24-h systolic BP all independently predicted cardiovascular events. However, only night-time systolic BP independently predicted cardiovascular mortality [7].

While these studies have all been generally suggestive that ABPM is prognostically superior to CBPM in the elderly, so far only the Syst-Eur trial has been able to demonstrate that ABPM predicts mortality independently of CBPM [7]. One reason for this is that the number of cardiovascular deaths in each of these three studies was relatively small; 34, 41 and 22 respectively; as opposed to 246 in this study [3, 4, 7]. Our results add significantly to those of the other authors by demonstrating that 24-h, daytime and night-time ambulatory SBP all significantly predict cardiovascular mortality over and above the clinic BP in a large elderly hypertensive population. Figure 1 shows the adjusted 5-year risk of cardiovascular death for a given BP and demonstrates the steeper increment in cardiovascular risk associated with increased ambulatory as opposed to clinic BP.

There has been increasing interest in the prognostic significance of nocturnal BP in recent years. Typically, BP falls by about 10–20% during sleep. It was first suggested in 1988 that a reduction in this normal nocturnal fall in BP, termed ‘non-dipping’, may be associated with an

increased risk of stroke [13]. Since then several studies have demonstrated increased cardiovascular events in individuals with a ‘non-dipping’ pattern of BP [7, 16–18]. It has also been shown that older people are more likely to be ‘non-dippers’ [28]. However, studies assessing the significance of nocturnal BP in the elderly have produced conflicting results. In the Syst-Eur trial, a higher night-time BP and an increased night-day ratio both independently predicted cardiovascular events [7]. However, other authors found no association between night-time BP and outcome in the elderly [3, 4]. In this study, of all the BP parameters, night-time BP was the most potent predictor of mortality. This was most marked for cerebrovascular events and a 10-mg rise in night-time SBP increased the risk of fatal stroke by 24%. Several Japanese studies have related ‘non-dipping’ with an increased risk of ischaemic stroke [15, 17, 29]. The results of our study and these others raise the hypothesis as to whether treatment targeted at nocturnal BP may be a more effective strategy to prevent stroke and cardiac events in older hypertensive patients.

Patterns of BP change with increasing age, with a higher prevalence of isolated systolic hypertension in the elderly. The relative prognostic significance of systolic and diastolic BP may also vary with age [1, 4, 30]. A high diastolic BP is associated with increased cardiovascular morbidity in younger people, whereas data from the Framingham study suggested a negative relationship between diastolic BP and mortality in those over 60 years. [30]. Similarly, Khattar

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*et al* reported a negative correlation between ambulatory diastolic BP and cardiovascular events in hypertensive patients over 60 and a positive correlation in those aged less than 60 [4]. In contrast, our results for this analysis of patients aged over 65 were similar to those we have previously reported for the entire population of the Dublin Outcome Study in that both diastolic and systolic ABPM were positively associated with cardiovascular mortality [10]. In keeping with this, Hansen *et al* found a positive association between ambulatory DBP and mortality in all age groups including the elderly in a large Danish population [12].

A potential limitation to our study is that deaths may not have been identified because of patients leaving the jurisdiction or changing names as a consequence of marriage. However, given the mean age of the patients these occurrences are not likely to have been significant. We adjusted for most major cardiovascular risk factors but did not have the information to adjust for some known risk factors, such as family history and cholesterol levels. In addition, we did not have sufficient data on anti-hypertensive medication during follow-up to adjust for the potential effect of treatment on outcome.

This is the largest analysis to date of ABPM and outcome in elderly patients. The evident superior prognostic power of ABPM, and particularly night-time BP, over CBPM makes a strong case for the routine use of 24-h ambulatory monitoring in older patients with an elevated clinic BP. Systolic BP increases with age and the elderly are at higher absolute risk of cardiovascular events than younger people making BP control of prime importance. However, treatment is complicated by the greater risk of side-effects from anti-hypertensive medication in the elderly. In addition, the increased prevalence of white-coat hypertension in older people means that clinic BP measurement may be less reliable [2]. This is consistent with our findings that a 10-mmHg rise in clinic BP was not associated with a significant increase in mortality risk in this group of patients aged over 65, whereas it was in younger people [10].

ABPM appears to be well tolerated in the elderly and its use has several advantages. Most importantly it will more accurately predict a patient's risk of a future fatal cardiovascular event allowing more precise definition of the risk-benefit equation regarding treatment. Secondly, it provides information about the circadian variability in BP. Thirdly, it obviates the need for repeated CBPMs in order to establish a diagnosis, allowing more rapid identification of patients requiring treatment.

In summary, we have demonstrated in a large elderly hypertensive population that ABPM provides prognostic information over and above CBPM, that CBPM alone is not a good predictor of outcome, and that night-time BP is the strongest predictor of mortality. In the future, randomised controlled trials are needed to determine whether treatment targeted at ambulatory and particularly night-time BP will improve outcome. For the reasons outlined above, it will be important to consider older people as a separate group in

these trials and also to separate patients aged 65–80 from those over 80 in whom the benefits of anti-hypertensive treatment have yet to be clearly defined [31].

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### Key points

- ABPM predicts cardiovascular mortality independently of clinic BP in hypertensive patients aged over 65.
- Clinic BP measurement alone was not a good predictor of outcome and a 10-mmHg rise in clinic systolic BP was not associated with a significant increase in mortality risk.
- Night-time BP is the strongest predictor of mortality in this age-group and provides additional prognostic information over and above the daytime BP.

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### Conflict of interest

None of the authors has a conflict of interest to declare.

### Acknowledgements

The assistance given by the General Register Office, Department of Health and Children, Dublin, Ireland is acknowledged with gratitude.

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Received 28 February 2007; accepted in revised form  
24 September 2007