

## ORIGINAL ARTICLE

# Treatment of hypertension in rural Cambodia: results from a 6-year programme

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This study was aimed to describe the outcomes of a hypertension treatment programme in two outpatient clinics in Cambodia. We determined proportions of patients who met the optimal targets for blood pressure (BP) control and assessed the evolution of mean systolic and diastolic BP (SBP/DBP) over time. Multivariate analyses were used to identify predictors of BP decrease and risk factors for LTFU. A total of 2858 patients were enrolled between March 2002 and June 2008 of whom 69.2% were female, 30.5% were aged  $\geq 64$  years and 32.6% were diabetic. The median follow-up time was 600 days. By the end of 2008, 1642 (57.4%) were alive-in-care, 8 (0.3%) had died and 1208 (42.3%) were lost to follow-up. On admission, mean SBP and DBP were 162 and 94 mm Hg, respectively. Among the patients treated, a significant SBP reduction of 26.8 mm Hg (95% CI:

28.4–25.3) was observed at 6 months. Overall, 36.5% of patients reached the BP targets at 24 months. The number of young adults, non-overweight patients and non-diabetics reaching the BP targets was more. Older age ( $> 64$  years), uncontrolled DBP ( $\geq 90$  mm Hg) on last consultation and coming late for the last consultation were associated with LTFU, whereas non-diabetic patients were 1.5 times more likely to default than diabetics (95% CI: 1.3–1.7). Although the definite magnitude of the BP decrease due to antihypertension medication over time cannot be assessed definitely without a control group, our results suggest that BP reduction can be obtained with essential hypertension treatment in a large-scale programme in a resource-limited setting.

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## Introduction

In 2005, the World Health Organisation (WHO) highlighted the importance of chronic diseases as a neglected global health problem.<sup>1</sup> In most countries the poorest people have the highest risk of developing chronic diseases and they are least able to cope with the resulting financial consequences.<sup>2</sup> Recently, the burden of chronic diseases was assessed in 23 selected low- and middle-income countries, and it was shown that they were responsible for 50% of the total disease burden in 2005. Moreover, the assessment showed that the estimated death rates from chronic diseases in the

low- and middle-income countries were higher than those in high-income countries.<sup>3</sup>

Hypertension is one of the most common risk factors for cardiovascular disease and has one of the highest attributable risks for death, worldwide.<sup>4,5</sup> Hypertension control remains poor in most clinical settings, despite the existence of several national and international guidelines on diagnosis and management.<sup>6</sup> For instance, in one study half of the patients with hypertension in industrialized countries reported receiving antihypertensive drugs, but only one-third of them had their blood pressure (BP) controlled to the recommended target of  $< 140/90$  mm Hg.<sup>7</sup> The situation is much worse in most developing countries where BP control rates are often (but not always) disappointingly low.<sup>8–10</sup> Unfortunately, the quality of information from these contexts is weak as most published studies are cross-sectional surveys and they do not report treatment outcomes over time, nor do they describe treatment programmes.

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In Cambodia, recent surveys have shown an unexpectedly high prevalence of arterial hypertension even in the relatively poor and traditional rural communities.<sup>11</sup> The prevalence of hypertension was 12% in a rural community (Siem Reap) and 25% in a semi-urban community (Kampong Cham), while access to care for this condition was and still is almost non-existent in most public health facilities.

In 2002 Médecins Sans Frontières Belgium, in collaboration with the Cambodian Ministry of Health, initiated a programme to provide care for patients with hypertension and diabetes in two rural settings, Siem Reap and Takeo provinces. The similarities between the management of these chronic conditions and HIV/AIDS led to the establishment of two Chronic Disease Clinics offering care for HIV/AIDS, including antiretroviral treatment, as well as care for diabetes and hypertension and a few other chronic conditions (asthma, epilepsy, arthritis and so on). This model of care showed the feasibility of integrating care for chronic diseases with that of HIV/AIDS and resulted in excellent clinical and immunological outcomes for the AIDS patients on antiretroviral treatment and encouraging outcomes for diabetic patients.<sup>12,13</sup> Nevertheless, the effectiveness of the hypertension treatment programme has not been fully assessed. This paper is unique in reporting the results of treating hypertensive patients over time as well as describing the model of care. The purpose of this report is to describe the results and challenges of a hypertension treatment programme in two rural outpatient clinics in Cambodia.

## Patients and methods

### *Setting*

The hypertension care programme was initiated in March 2002 in the Siem Reap province (population 700 000) and one year later in the Takeo province (population 800 000) in Cambodia. Care was offered on an outpatient clinic basis. The clinics were located at the public referral hospitals and operated similarly in both locations.

### *Study population*

Adult patients diagnosed with hypertension between March 2002 and June 2008 were enrolled in the Takeo and Siem Reap Chronic Disease Clinics. Only patients who returned at least once after their first consultation were considered as having 'enrolled' in the programme and were included in the study. Two BP measurements were taken at each of these two first visits and were reported at patients' records, but only BP values at enrolment (during the second visit) were considered as baseline BP. Patient admissions were somewhat restricted in 2007 due to high workload.

### *Programme description*

We provided integrated patient-centred care for hypertensive patients with and without diabetes, in the same clinic that cared for HIV-positive patients, as has already been described.<sup>12</sup> Patients with hypertension were either self-referred or referred by public or private health service providers. The Chronic Disease Clinic staff included general practitioners, nurses, drug educators, adherence counsellors, a receptionist and support staff to facilitate patient flow. All staff were trained in hypertension and diabetes care. MSF subsidized care so that patients were required to pay for initial registration (one USD), for antihypertensive and diabetic drugs until mid 2005 (at a subsidized price) and for transportation. However, from mid 2005 onwards, all drugs were free of charge. The programme never covered transportation costs for patients.

### *Standardized care and follow-up procedures*

The criteria for diagnosis of hypertension were systolic BP (SBP)  $\geq 140$  mm Hg and/or diastolic BP (DBP)  $\geq 90$  mm Hg on at least two occasions (two separate visits). Patients diagnosed with hypertension by a qualified provider and on antihypertensive treatment were also registered in the clinic. Patients were seen first by a nurse and then, if control was not achieved, by a medical doctor. During the first consultation, history, physical examination and management planning were recorded in an individual patient file. Two BP measurements at first visit and at all follow-up visits were performed after patients rested for 5–10 min and while lying on a bed. BP readings were routinely made by nurses. Medical doctors performed BP measurements only on selected cases (uncontrolled BP, unexplained fluctuation of BP) and always after the nurses' readings. The second reading by the nurse (or a third by a medical doctor if this was the case) was routinely recorded. Manual mercury sphygmomanometers were used in the clinics. Cuffs of two different sizes were available to accommodate differing arm circumferences. After late 2006 aneroid sphygmomanometers were also used to cope with the heavier clinic workload. Verification of these machines using mercury sphygmomanometers was regularly performed by the clinic staff.

Glucose levels were measured with a glucometer (OneTouch; LifeScan Inc., Milpitas, CA, USA) using capillary blood for all patients during the initial consultation and upon clinical suspicion of diabetes during follow-up visits. Systematic measurement of glycated haemoglobin (HbA1c) for diabetic patients at baseline and on a quarterly basis was performed after May 2007 (high-performance liquid chromatography; Bio-Rad D-10, Hercules, CA, USA). For body mass index (BMI) the WHO reference points for Asian populations were used: 23–27.5 kg m<sup>-2</sup> defined as 'overweight' and 27.5 kg m<sup>-2</sup> or above, as 'obesity'.<sup>14</sup>

Advice on exercise, smoking cessation, low salt intake and appropriate diet was given to all patients on an individual basis, by the doctors in the early years of the programme (until 2005) and thereafter by the counsellors. Patients without target organ damage were under non-pharmacological care. Patients with target organ damage were started on mono-therapy and progressed to bi-therapy and tri-therapy if BP target was not reached with mono-therapy. The prescribed agents were generic formulations of the following drug classes: thiazide diuretics,  $\beta$ -blockers, angiotensin-converting enzyme inhibitors and  $\text{Ca}^{++}$  blockers. BP targets were  $<140/90$  mm Hg for non-diabetic patients and  $<130/80$  mm Hg for diabetic patients.

For diabetic patients an oral hypoglycaemic agent was administered: metformin if  $\text{BMI} \geq 23 \text{ kg m}^{-2}$  and glibenclamide if  $\text{BMI} < 23 \text{ kg m}^{-2}$  or if contraindications to metformin. Two diabetes drugs were used for patients failing to reach glucose control with mono-therapy. Insulin therapy was only reserved for patients with moderate-to-severe renal impairment.

Non-pharmacotherapy patients were followed up on a bi-monthly basis. Patients on pharmacotherapy were initially followed up bi-weekly, then every 1–3 months according to their WHO stage, existing comorbidities and risk factors for cardiovascular diseases. At each follow-up visit, BP, weight/BMI and blood sugar were monitored for diabetic patients; treatment acceptance, tolerance and adherence were checked with open-ended questions; and assessment for complications was performed. Adherence to medication was self-reported. Due to limited resources, we were not able to introduce an electronic medication monitoring system that could have provided more objective measurements of adherence. If drug intake was irregular, patients received counselling sessions and support from the clinic's nurse counsellors and drug educators.

#### Data collection

Clinical information was systematically recorded on standardized clinical files designed specifically for the programme. Information was prospectively collected and entered into a software application developed locally, specifically for chronic diseases. Trained personnel extracted clinical, treatment and laboratory data from individual patient records daily and entered them into the database. A full-time data manager routinely checked data entry for accuracy and completeness.

#### Statistical analysis

Data from all adult patients diagnosed with hypertension between March 2002 and June 2008, and enrolled in the Takeo and Siem Reap Chronic Disease Clinics were used in the analyses. Patients had to have returned at least once after the first consultation to be considered as having enrolled in

the programme. For the purposes of this analysis, the date of enrolment of diabetic hypertensive patients corresponded to the time when they were diagnosed with hypertension, independently of when this occurred during diabetes treatment.

Patient characteristics at admission and their status at the end of the study period were summarized using descriptive statistics. We assessed the evolution of the mean SBP and DBP over treatment time separately for non-diabetic and diabetic hypertensive patients. Paired *t*-test was used to compare baseline and subsequent paired values of BP.

To analyse the effect of various factors on BP decrease over time, we performed a linear regression on BP difference at month 12 of follow-up, separately for SBP and DBP. The explanatory variables included baseline BP, age group, sex and the timeliness of last consultation, diabetes, BMI and type of treatment.

A patient was defined as lost-to-follow-up if he/she had missed a scheduled appointment by over 3 months and was not known to be dead or had not transferred-out. Only patients who attended at least two consultations were included in the analysis of risk factors for loss to follow-up (LTFU). Potential risk factors for LTFU, including sex, age, diabetes comorbidity, year of admission, geographical origin, last SBP and DBP, and last consultation (late or not late), were assessed using a Cox regression model.

Data were analysed using Excel and STATA 8.2 (STATA Corp., College Station, TX, USA). The study protocol was approved by the National Ethics Committee for Health Research of Cambodia and the Ethics Review Board of Médecins Sans Frontières in January 2009.

## Results

#### Patient characteristics

There were 2858 ambulatory patients diagnosed with hypertension enrolled in the two clinics between March 2002 and June 2008. The majority of patients were self-referred and known to have high BP. The characteristics of patients at first consultation are shown in Table 1. Patients were predominantly females (69.2%), and more than 60% were  $\geq 55$  years old. On admission, mean SBP and DBP were 162 and 94 mm Hg, respectively, while 91.2% of patients had elevated SBP and 76.7% had elevated DBP. At the same time, 62% of the patients were overweight and 22% were obese.

Of patients with type-II diabetes, 931 were diagnosed with hypertension in the two clinics and included in the analysis. Characteristics at first consultation of diabetic patients with hypertension were similar to those of non-diabetic patients with hypertension (Table 1). The median first random blood glucose measurement for diabetic patients was 257 mg/dl and the median first glycated haemoglobin was 11.4%.

**Table 1** Characteristics of hypertensive patients enrolled in care

	Hypertension only	Diabetes with hypertension	Total
Number of patients registered	1927	931	2858
Age in years, median (IQR)	58 (50–67)	57 (51–65)	58 (50–66)
Age group in years, <i>n</i> (%)			
<35	1.6%	0.5%	1.3%
35–44	10.7%	8.3%	9.9%
45–54	26.0%	28.8%	26.9%
55–64	29.2%	36.1%	31.4%
>64	32.5%	26.3%	30.5%
Women, <i>n</i> (%)	68.7%	70.3%	69.2%
Blood pressure			
Systolic, mean (s.d.)	162 (25)	162 (18)	162 (23)
Diastolic, mean (s.d.)	93 (13)	95 (11)	94 (12)
% with systolic BP $\geq 140$ mm Hg	88.2%	97.1%	91.2%
% with diastolic BP $\geq 90$ mm Hg	72.2%	85.6%	76.7%
BMI (kg/m <sup>2</sup> ), median (IQR)	24.0 (21.2–27.0)	24.4 (21.9–27.0)	24.2 (21.5–27.0)
% overweight with BMI $\geq 23.0$	60.5%	65.3%	62.3%
% obese with BMI $\geq 27.5$	21.8%	21.8%	21.8%

Abbreviations: BMI: body mass index; BP, blood pressure; IQR, inter-quartile range.

The second BP readings during the second clinic visit were recorded as baseline SBP and DBP.

### Treatment and follow-up

The median follow-up period per patient was 600 days. The follow-up time was longer for diabetic patients than for non-diabetic patients (median 21 versus 19 months). Approximately 57 and 14% of patients were prescribed two and three or more oral antihypertensive drugs, respectively, at their last consultation. The most commonly prescribed agents were thiazide diuretics (1506),  $\beta$ -blockers (1283), angiotensin-converting enzyme inhibitors (1083), whereas  $\text{Ca}^{++}$  blockers (366) were prescribed mostly during the last year of the programme.

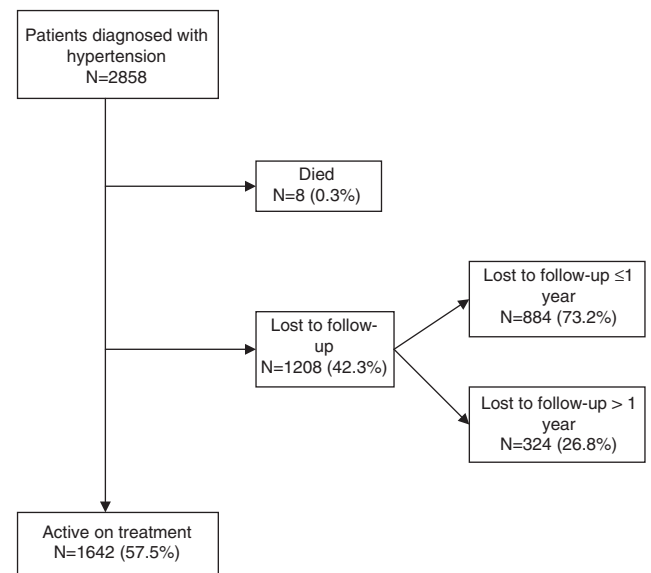
### Cohort outcomes

By the end of the observation period (December 2008), 1642 (57.5%) patients were alive and in care, 8 (0.3%) had died and 1208 (42.3%) were lost to follow-up (Figure 1). Most LTFU (73.2%) occurred within the first year after enrolment.

### BP control

Overall, 36.5% of all patients and 49.3% of non-diabetic hypertensive patients reached the BP target at 24 months. Of the non-diabetic patients, 51.4% of female patients and 58.9% of patients aged <55 years reached the BP target at 24 months. Only 12.3% of diabetic hypertensive patients reached their BP target at 24 months.

Figure 2 illustrates the evolution of the mean SBP and DBP values over treatment time. The initial reduction observed during the first six months of treatment was maintained over the 5-year period. *t*-Test for paired values showed a significant decrease in BP between first consultation and 6 months ( $P < 0.001$ ) among diabetic and non-diabetic pa-

**Figure 1** Flowchart of patients with hypertension diagnosed in March 2002–June 2008 at the end of the study period.

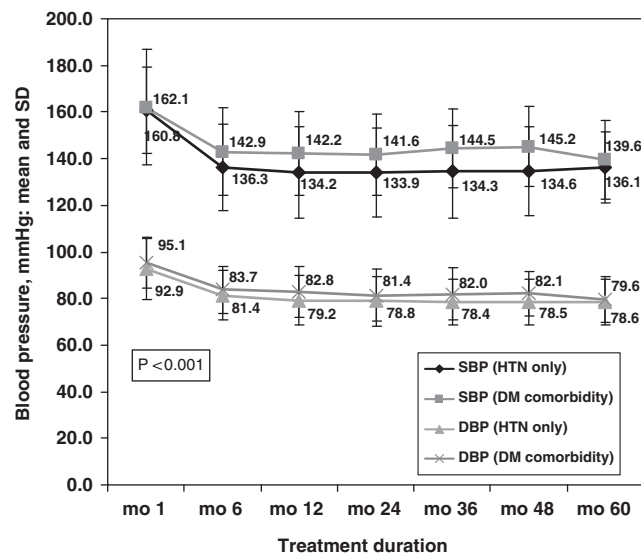
tients. The largest decrease was observed in non-diabetic patients: an SBP decrease of 26.8 mm Hg (95% confidence interval (CI): 28.4–25.3) between first consultation and 6 months.

After adjusting for all factors, the multivariate linear regression analysis showed a positive relationship between baseline SBP and SBP decrease at month 12 and a negative relationship between age group, BMI, diabetes and SBP decrease at month 12. Decreased SBP after 12 months of treatment was positively correlated to increased SBP at baseline, younger age group, decreasing BMI and absence of diabetes (Tables 2a and b). Sex, timeliness of last consultation and number of antihypertensive drugs

at last consultation did not show a linear relationship with SBP or DBP decrease at month 12.

#### Risk factors for LTFU

A total of 2778 hypertensive patients registered from 2002 to 2008 who had attended at least two clinic



**Figure 2** Evolution of mean (s.d.) of BP in patients with hypertension according to diabetes comorbidity. BP, blood pressure.

consultations were included in the analysis of risk factors for LTFU. All factors with a  $P$ -value  $< 0.05$  in the univariate analysis were entered in the multivariate Cox regression model (Table 3). Older age ( $> 64$  years), uncontrolled DBP ( $\geq 90$  mm Hg) on last consultation and coming late for the last consultation were significantly associated with LTFU. Diabetes comorbidity was a significant protective factor for retention in care. Patients without diabetes were 1.5 times more likely to default than diabetes patients (95% CI: 1.3–1.7).

## Discussion

The treatment outcomes of this large cohort of patients receiving standardized care in a resource-limited setting with high prevalence of hypertension are encouraging. However, these results should be interpreted carefully as there was no control group and the magnitude of the BP decrease due to antihypertension medication cannot be definitely assessed. Overall, significant decreases in BP were observed in patients within 6 months of treatment and lower BP levels were maintained throughout the study period. However, the majority of patients did not reach the recommended targets for optimal SBP control. In light of the evidence that a decrease in BP is associated with a decreased risk for cardiovascular disease and mortality in individuals with arterial hypertension,<sup>15–17</sup> it is highly likely that patients

**Table 2a** Univariate and multivariate linear regression analysis on SBP decrease after 12 months of treatment ( $n = 1260$ )

Explanatory variables	Univariate analysis		Multivariate analysis adjusting for all factors	
	Regression coefficient (95% CI) P-value		Regression coefficient (95% CI) P-value	
Baseline systolic BP	0.99 (0.96 to 1.04)	<0.001	1.00 (0.96 to 1.05)	<0.001
Age group:	–4.50 (–6.86 to –2.15)	<0.001	–4.98 (–6.68 to –3.27)	<0.001
1: <45 years				
2: 45–64 years				
3: >64 years				
Sex	–1.45 (–4.49 to 1.58)	0.347	0.52 (–1.67 to 2.70)	0.642
0: male				
1: female				
Timeliness of last consultation:	–3.39 (–6.74 to –0.05)	0.047	–0.93 (–3.43 to 1.58)	0.468
1: on time				
2: late				
Diabetes:	–9.38 (12.26 to –6.50)	<0.001	–7.64 (–9.76 to –5.52)	<0.001
0: no diabetes				
1: diabetes				
BMI	–0.14 (–0.38 to 0.10)	0.251	–0.33 (–0.54 to –0.13)	0.001
Number of BP drugs:	3.95 (1.88 to 6.02)	<0.001	–0.589 (–2.00 to 0.83)	0.414
1 drug				
2 drugs				
3 drugs				
4 drugs				

Abbreviations: BMI: body mass index; BP, blood pressure; CI, confidence interval; SBP, systolic blood pressure.



**Table 2b** Univariate and multivariate linear regression analysis on DBP decrease after 12 months of treatment ( $n = 1260$ )

Explanatory variables	Univariate analysis		Multivariate analysis adjusting for all factors	
	Regression coefficient (95% CI) P-value		Regression coefficient (95% CI) P-value	
Baseline diastolic BP	1.01 (0.97 to 1.05)	<0.001	0.98 (0.92 to 1.03)	<0.001
Age group:	1.61 (0.32 to 2.90)	0.014	1.18 (0.19 to 2.18)	0.1866994
1: <45 years				
2: 45–64 years				
3: >64 years				
Sex:	–1.50 (–3.15 to 0.15)	0.075	0.79 (–0.49 to 2.08)	0.225
0: male				
1: female				
Timeliness of last consultation:	–2.56 (–4.38 to –0.73)	0.006	–0.82 (–2.29 to 0.65)	0.272
1: on time				
2: late				
Diabetes:	–3.79 (–5.37 to –2.21)	<0.001	–3.57 (–4.81 to –2.32)	<0.001
0: no diabetes				
1: diabetes				
BMI	0.16 (0.03 to 0.29)	0.014	–0.02 (–0.14 to 0.10)	0.710
Number of antihypertensive drugs:	1.86 (0.74 to 2.99)	0.001	0.073 (–0.75 to 0.90)	0.862
1 drug				
2 drugs				
3 drugs				
4 drugs				

Abbreviations: BMI: body mass index; BP, blood pressure; C, confidence interval; DBP, diastolic blood pressure.

with decreased BP gained clinical benefit even if they did not reach their target. The fact that younger patients (aged <55 years) responded better to treatment is reassuring as the medical consequences of uncontrolled hypertension in these individuals are worse than those in the older age group.

Previous studies, in both high- and low-resource countries, have shown that treatment targets for BP are difficult to reach in clinical practice. Large patient studies in industrialized countries have found relatively low proportions (27–34%) of hypertensive patients with fully controlled BP, although a few surveys do show better results (48–63%).<sup>18–25</sup> Quantitative data on BP control among hypertensive patients treated in middle- and low-income countries are more limited and certainly no better (19.5–44.4%).<sup>26–31</sup> A recent systematic review of the literature found no significant differences in mean prevalence, awareness, treatment and control of hypertension between developing and developed countries.<sup>10</sup> However, a previous systematic review of population-based studies on hypertension in sub-Saharan Africa between 1975 and 2006 found that among patients with previously diagnosed hypertension, less than 30% were on drug treatment in most studies, and less than 20% had their BP controlled.<sup>32</sup> Both reviews identified a discouragingly low number of scientific publications on hypertension from resource-limited settings, and published studies, other than cross-sectional surveys, are more scarce.<sup>33</sup>

Original studies on the association between hypertension control and sex have been contradictory. Several studies reported that men achieved better control, others showed that female sex is a predictor of treatment success and some found no differences between the sexes.<sup>34–38</sup> In our study, no significant differences of BP control between men and women under treatment were found over time. However, 70% of our patients were women and this finding is consistent with a systematic review that showed that in developing countries, overall, women were more aware of their hypertension status and more likely to get pharmacological treatment.<sup>10</sup>

The reasons for less-than-optimal BP control results are multi-factorial and include poor adherence to taking medication, poor weight control, half-hearted lifestyle modifications and lack of therapy intensification. The latter could also be seen as a combination of low aggressiveness in hypertension management by clinicians and the difficulties in introducing new classes of antihypertensive drugs, which are either unavailable or unaffordable in resource-limited settings. The issue of adherence to treatment is central for long-term control of BP, but often less than 50%, or even less than 30% of patients, take their medication regularly.<sup>39</sup> In our cohort, one-third of patients were diabetics and BP control among them was worse when compared with non-diabetic patients. Stricter treatment targets for diabetic hypertensive patients (130/80 versus 140/90) may partly explain this difference.

**Table 3** Univariate and multivariate Cox regression analysis of risk factors for LTFU among all hypertensive patients<sup>a</sup> (*n* = 2778)

<i>Factors</i>	<i>No. lost to follow-up/ follow-up time</i>	<i>HR</i>	<i>95% CI</i>	<i>P-value</i>	<i>aHR<sup>b</sup></i>	<i>95% CI</i>	<i>P-value</i>
<i>Sex</i>							
Male	23.4%	1			1		
Female	19.9%	0.85	0.75–0.96	0.0076	0.99	0.88–1.12	0.902
<i>Age (years)</i>							
≤ 64	16.6%	1			1		
> 64	34.2%	2.06	1.84–2.31	<0.001	1.78	1.58–2.01	<0.001
<i>Diabetes</i>							
Yes	16.1%	1			1		
No	23.8%	1.48	1.30–1.67	<0.001	1.51	1.33–1.71	<0.001
<i>Origin</i>							
Inside province	21.8%	1	0.98–1.66				
Outside province	27.8%	1.28		0.065			
<i>Treatment centre</i>							
Siem Reap	20.2%	1			1		
Takeo	23.0%	1.14	1.00–1.29	0.0399	1.09	0.96–1.25	0.186
<i>Year of admission</i>							
2002	18.1%	1			1		
2003–2008	20.9%	1.08 <sup>c</sup>	1.04–1.12	0.002	0.97	0.93–1.01	0.147
<i>Last SBP (mm Hg)</i>							
< 140	16.2%	1			1		
≥ 140	24.5%	1.51	1.34–1.70	<0.001	1.11	0.97–1.28	0.129
<i>Last DBP (mm Hg)</i>							
< 90	16.3%	1			1		
≥ 90	32.9%	2.02	1.80–2.27	<0.001	1.78	1.56–2.05	<0.001
<i>Timeliness of last consultation</i>							
On time	15.5%	1			1		
Late	42.1%	2.71	2.42–3.04	<0.001	2.24	1.99–2.53	<0.001

Abbreviations: aHR, adjusted hazards ratio; CI, confidence interval; DBP, diastolic blood pressure; HR, hazards ratio; LTFU, loss to follow-up; SBP, systolic blood pressure.

<sup>a</sup>Included all patients registered between March 2002 and June 2008, and attended at least two consultations.

<sup>b</sup>All factors with *P*-value < 0.05 in univariate analysis were included in the multivariable regression model. *P*-value for the likelihood ratio test for the model was < 0.001.

<sup>c</sup>Score test for trend of rates with an estimate of rate ratio for a one unit increase in year.

Additionally, it is well known that effective BP control can be difficult to achieve in diabetes.<sup>17</sup>

A high proportion of our patients were overweight or obese at first consultation. The weight control results in our cohort were poor, especially for diabetes (data not shown), and this could be, in part, due to insufficient and inadequate patient education. Lifestyle changes, implying behavioural and environmental change, are known to be difficult to promote effectively in a clinic setting. Moreover, in our context we could not exclude a cultural reluctance to lose weight, as there is no dietary advice and no promotion of physical exercise at the population level in the country.

In our settings we were seriously limited in screening for and treatment of major complications related to hypertension, especially cardiovascular disease. Lack of experienced physicians and lack of access to appropriate diagnostics may have resulted in serious gaps in diagnosing such complications.

Limited financial resources also prevented us from systematically introducing lipid-lowering agents in our protocols, as these drugs remained prohibitively expensive and not widely available in Cambodia.

The high LTFU observed among patients with hypertension strikingly contrasts with the low LTFU documented among HIV/AIDS patients on antiretroviral treatment treated at the same clinic (cumulative LTFU of 3% over 5 years). One contributing factor could be the inequality in care: HIV/AIDS patients received free health care, money for transportation, food and social support, whereas hypertensive patients did not get any of these benefits.<sup>40,41</sup> In our cohort, patients 64 years or older, patients late for their last appointment and those with poor SBP control during their last visit were more likely to be lost to follow-up. Older patients are unlikely to work and depend on family members for living and health expenditures, such as transport and drugs, over which they have no

control. Another factor is that hypertensive patients, contrary to HIV patients, have several alternatives for care such as traditional medicine and local pharmacies. Antihypertensive medicines similar to the ones provided by the clinics can be bought at local pharmacies thereby saving travel costs and time. Finally, the weakness of the counselling and patient education components of care probably led to an insufficient understanding by patients of the disease and its consequences if untreated, leading to reduced motivation to continue treatment.

This study had certain limitations. First, even though data were collected on standardized patient forms and entered prospectively into a specifically designed software programme, errors or omissions could have occurred, as data were collected from a routine clinic and not specifically for research purposes. Second, we acknowledge that we only used biological measurements, as surrogate markers, for hypertension treatment outcomes. The lack of access to specialized diagnostics and care for complications and lack of standardized case definitions prevented us from collecting information about them, as mentioned above. Third, deaths were likely underestimated in our cohort and misclassified as LTFU, as we had no means of checking on defaulters. Fourth, we acknowledge that regression to the mean and habituation to repeated BP measurements could have had an effect on the decrease in BP observed during follow-up.<sup>42</sup> Without control cases the specific effect of antihypertensive treatment cannot be fully assessed. Despite these limitations, our study's strengths were its large size, relatively lengthy follow up, prospective data collection and use of specialized software.

In conclusion, the findings of this study suggest that improvement in BP control can be obtained in individuals with essential hypertension treated in a low-resource setting. Although the exact magnitude of the BP decrease due to antihypertension medication over time cannot be definitely assessed without a control group, our results do offer encouragement for scaling up care for chronic diseases like hypertension, as they are a large and growing burden of illness in the developing countries.

#### What is known about the topic

- Hypertension control remains poor in most clinical settings, despite the existence of several guidelines on diagnosis and management.
- The outcomes of hypertensive patients treated in resource-limited setting remain largely undocumented.

#### What this study adds

- Encouraging improvement in BP control can be obtained in hypertensive individuals treated in a resource-limited setting.
- LTFU is an challenging issue in hypertension care programs and better strategies are needed to improve long-term retention in care.

## Conflict of interest

The authors declare no conflict of interest.

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## References

- 1 WHO. *Preventing chronic diseases: a vital investment: WHO global report*. World Health Organization: Geneva, 2005.
- 2 Suhrcke M, Nugent RA, Stuckler D, Rocco L. *Chronic Diseases: an Economic Perspective*. The Oxford Health Alliance: London, 2006.
- 3 Abegunde D, Mathers CD, Adam T, Ortegon M, Strong K. The burden and costs of chronic diseases in low-income and middle-income countries. *Lancet* 2007; **370**: 1929–1938.
- 4 Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet* 2006; **367**: 1747–1757.
- 5 He J, Gu D, Wu X, Reynolds K, Duan X, Yao C *et al*. Major causes of death among men and women in China. *N Engl J Med* 2005; **353**: 1124–1134.
- 6 Hypertension Detection and Follow-up Program Cooperative Group. Five-year findings of the hypertension detection and follow-up program: I. Reduction in mortality of persons with high blood pressure, including mild hypertension. *JAMA* 1997; **277**: 157–166.
- 7 Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988–2000. *JAMA* 2003; **290**: 199–206.
- 8 Wang Z, Wu Y, Zhao L, Li Y, Yang J, Zhou B. Trends in prevalence, awareness, treatment and control of hypertension in the middle-aged population of China, 1992–1998. *Hypertens Res* 2004; **27**: 703–709.
- 9 Jafar TH, Levey AS, Jafary FH, White F, Gul A, Rahbar MH *et al*. Ethnic subgroup differences in hypertension in Pakistan. *J Hypertens* 2003; **21**: 905–912.
- 10 Pereira M, Lunet N, Azevedo A, Barros H. Differences in prevalence, awareness, treatment and control of hypertension between developing and developed countries. *J Hypertens* 2009; **27**: 963–975.
- 11 King H, Lim K, Seng S, Khun T, Roglic G, Pinget M. Diabetes and associated disorders in Cambodia; two epidemiological surveys. *Lancet* 2005; **366**: 1633–1639.
- 12 Janssens B, Van Damme W, Raleigh B, Gupta J, Khem S, Soy Ty K *et al*. Offering integrated care for HIV/AIDS, diabetes and hypertension within chronic disease clinics in Cambodia. *Bull World Health Organ* 2007; **85**(11): 880–885.
- 13 Raguenaud M-E, Isaakidis P, Reid T, Chy S, Keuky L, Arellano G *et al*. Treating 4000 diabetic patients in Cambodia, a high prevalence but resource-limited setting: a five-year study. *BMC Med* 2009; **7**: 33.



- 14 WHO Expert consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004; **363**: 157–163.
- 15 Messerli FH, Williams B, Ritz E. Essential hypertension. *Lancet* 2007; **370**(9587): 591–603.
- 16 Williams B. Recent hypertension trials: implications and controversies. *J Am Coll Cardiol* 2005; **45**(6): 813–827.
- 17 Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G *et al*. Guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2007; **28**(12): 1462–1536.
- 18 Mitka M. Research probes details of poor adherence in antihypertensive drug therapy. *JAMA* 2007; **298**(18): 2128.
- 19 Centers for Disease Control and Prevention (CDC). Racial/ethnic disparities in prevalence, treatment, and control of hypertension—United States, 1999–2002. *MMWR Morb Mortal Wkly Rep* 2005; **54**(1): 7–9.
- 20 Efstratopoulos AD, Voyaki SM, Baltas AA, Vratsistas FA, Kirlas DE, Kontoyannis JT *et al*. Prevalence, awareness, treatment and control of hypertension in Hellas, Greece: the Hypertension Study in General Practice in Hellas (HYPERTENSHELL) national study. *Am J Hypertens* 2006; **19**(1): 53–60.
- 21 Psaltopoulou T, Orfanos P, Naska A, Lenas D, Trichopoulos D, Trichopoulou A. Prevalence, awareness, treatment and control of hypertension in a general population sample of 26,913 adults in the Greek EPIC study. *Int J Epidemiol* 2004; **33**(6): 1345–1352.
- 22 Primatesta P, Brookes M, Poulter NR. Improved hypertension management and control: results from the health survey for England 1998. *Hypertension* 2001; **38**(4): 827–832.
- 23 Primatesta P, Poulter NR. Improvement in hypertension management in England: results from the health survey for England 2003. *J Hypertens* 2006; **24**(6): 1187–1192.
- 24 Lang T, de Gaudemaris R, Chatellier G, Hamici L, Diène E. Prevalence and therapeutic control of hypertension in 30,000 subjects in the workplace. *Hypertension* 2001; **38**(3): 449–454.
- 25 Scheltens T, Bots ML, Numans ME, Grobbee DE, Hoes AW. Awareness, treatment and control of hypertension: the ‘rule of halves’ in an era of risk-based treatment of hypertension. *J Hum Hypertens* 2007; **21**(2): 99–106.
- 26 Fasce E, Campos I, Ibáñez P, Flores M, Zárate H, Román O *et al*. Trends in prevalence, awareness, treatment and control of hypertension in urban communities in Chile. *J Hypertens* 2007; **25**(9): 1807–1811.
- 27 Wang Z, Wu Y, Zhao L, Li Y, Yang J, Zhou B. Trends in prevalence, awareness, treatment and control of hypertension in the middle-aged population of China, 1992–1998. *Hypertens Res* 2004; **27**(10): 703–709.
- 28 Li W, Jiang X, Ma H, Yu TS, Ma L, Puente JG *et al*. Awareness, treatment and control of hypertension in patients attending hospital clinics in China. *J Hypertens* 2003; **21**(6): 1191–1197.
- 29 Howteerakul N, Suwannapong N, Sittilert R, Rawdaree P. Health risk behaviours, awareness, treatment and control of hypertension among rural community people in Thailand. *Asia Pac J Public Health* 2006; **18**(1): 3–9. Links.
- 30 Hazarika NC, Narain K, Biswas D, Kalita HC, Mahanta J. Hypertension in the native rural population of Assam. *Natl Med J India* 2004; **17**(6): 300–304.
- 31 Lim TO, Morad Z. Prevalence, awareness, treatment and control of hypertension in the Malaysian adult population: results from the national health and morbidity survey 1996. *Singapore Med J* 2004; **45**(1): 20–27.
- 32 Addo J, Smeeth L, Leon DA. Hypertension in sub-Saharan Africa: a systematic review. *Hypertension* 2007; **50**(6): 1012–1018.
- 33 Isaakidis P, Swingler GH, Pienaar E, Volmink J, Ioannidis JP. Relation between burden of disease and randomised evidence in sub-Saharan Africa: survey of research. *BMJ* 2002; **324**(7339): 702.
- 34 Stockwell DH, Madhavan S, Cohen H, Gibson G, Alderman MH. The determinants of hypertension awareness, treatment, and control in an insured population. *Am J Public Health* 1994; **84**(11): 1768–1774.
- 35 Alexander M, Tekawa I, Hunkeler E, Fireman B, Rowell R, Selby JV *et al*. Evaluating hypertension control in a managed care setting. *Arch Intern Med* 1999; **159**: 2673–2677.
- 36 Knight EL, Bohn RL, Wang PS, Glynn RJ, Mogun H, Avorn J. Predictors of uncontrolled hypertension in ambulatory patients. *Hypertension* 2001; **38**(4): 809–814.
- 37 Hicks LS, Fairchild DG, Horng MS, Orav EJ, Bates DW, Ayanian JZ. Determinants of JNC VI guideline adherence, intensity of drug therapy, and blood pressure control by race and ethnicity. *Hypertension* 2004; **44**(4): 429–434.
- 38 Majernick TG, Zacker C, Madden NA, Belletti DA, Arcona S. Correlates of hypertension control in a primary care setting. *Am J Hypertens* 2004; **17**(10): 915–920.
- 39 Bovet P, Burnier M, Madeleine G, Waeber B, Paccaud F. Monitoring one-year compliance to antihypertension medication in the Seychelles. *Bull World Health Organ* 2002; **80**(1): 33–39.
- 40 Chean Rithy Men. Qualitative study on health care access among HIV/AIDS and diabetic patients in Cambodia. Research project supported by the European Commission. 2007 (EuropeAID, Health/2002/045-809).
- 41 Binagwaho A, Ratnayake N. The role of social capital in successful adherence to antiretroviral therapy in Africa. *PLoS Med* 2009; **6**(1): e18.
- 42 Bovet P, Gervasoni JP, Ross AG, Mkamba M, Mtasiwa DM, Lengeler C *et al*. Assessing the prevalence of hypertension in populations: are we doing it right? *J Hypertens* 2003; **21**(3): 473–474.