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**Title:**

Diagnosing hypertension in primary care: the importance of night-time blood pressure assessment

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## **ABSTRACT**

### **Background**

Ambulatory blood pressure monitoring (ABPM) has become less frequent in primary care since the COVID-19 pandemic, with home blood pressure monitoring (HBPM) often the preferred alternative; however, HBPM cannot measure night-time blood pressure (BP) and patients whose night-time BP does not dip or rises (reverse-dipping) have poorer cardiovascular outcomes.

### **Aim**

To investigate the importance of measuring night-time BP when assessing individuals for hypertension.

### **Design and Setting**

Retrospective cohort study of two patient populations; the first being hospital patients admitted to four UK acute hospitals and the second being participants of the BP-Eth study recruited from 28 UK GP practices.

### **Method**

Using blood pressure data collected for the two cohorts, we studied three systolic blood pressure (SBP) phenotypes (dipper, non-dipper and reverse-dipper).

### **Results**

Among the hospital cohort (n=21,739) 48.9% patients were 'reverse-dippers', with an average day-night SBP difference of -8.0 mmHg. Among the community cohort (n=585) 10.8% patients were 'reverse-dippers' with an average day-night SBP difference of -8.5 mmHg. Non-dipper and reverse-dipper phenotypes both have lower day-time SBP and higher night-time SBP than the dipper phenotype. Average day-time SBP was lowest in the reverse-dipping phenotype (6.5 mmHg and 6.8 mmHg lower than for the dipper phenotype in the hospital and community cohorts, respectively), thus placing them at risk of undiagnosed, or masked hypertension.

### **Conclusion**

Not measuring night-time BP puts all groups other than dippers at risk of failure to identify hypertension. We recommend that GPs should offer ABPM to all patients aged  $\geq 60$  as a minimum, when assessing for hypertension.

### **Keywords**

**Hypertension, blood pressure monitoring, ambulatory blood pressure monitoring, cardiovascular disease**

### **How this fits in:**

- Since the 1990s, the phenotypic classification of 24-hour blood pressure has divided the population into 'dippers', 'non-dippers' (minimal night-time BP decrease compared to day-time BP) and 'reverse dippers' (night-time BP increases compared to day-time BP).
- There is an established body of research demonstrating that reverse dippers are at higher risk of death and that the night-day systolic blood pressure ratio is an independent predictor of all cause mortality and cardiovascular events.
- Presently, UK guidelines suggest clinicians should diagnose hypertension based solely on daytime BP measurements.
- This study reveals a marked proportion of our population are reverse dippers; together with the established clinical research that has demonstrated worse cardiovascular outcomes for such patients, this highlights the need for 24-hour ambulatory blood pressure assessments to

detect and diagnose those with nocturnal hypertension, non-dipping or reverse-dipping blood pressure phenotypes.

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## 1. Introduction:

The circadian pattern of blood pressure and its pathophysiological impact have been studied extensively over the last few decades. The usual circadian pattern, which depends primarily on the sleep-wake cycle, consists of a decrease in blood pressure (BP) during sleep (described as a 'dipper pattern'), usually ascribed to reduction in sympathetic tone and increase in vagal activity.<sup>1</sup> This is then followed by a morning increase, and minor oscillations during the day.

The phenotypic classification of BP, dividing people into 'dippers' and 'non-dippers' (minimal night-time BP decrease compared to day-time BP), has been used since 1988.<sup>2,3</sup> Mention of a third phenotype ('reverse-dipper') appeared in the literature in the 1990s.<sup>4,5</sup> This characterises individuals whose average night-time BP is greater than their average day-time BP.

A study of 7,458 people in multiple countries<sup>4</sup> showed that night-time BP, adjusted for day-time BP, predicted total, cardiovascular and non-cardiovascular mortality. Reverse dippers were found to be older, were more likely to come from South America or Asia, and were at higher risk of death. A European study found that the night-day systolic BP (SBP) ratio independently predicted all-cause mortality and cardiovascular events, which persisted after additional adjustment for 24-h SBP.<sup>5</sup> Two very recent papers reach similar conclusions. A population-based study in which night-time BP was adjusted for day-time BP, showed night-time BP was a stronger prognostic predictor than day-time BP.<sup>8</sup> In a review studying the prevention, detection and management of high BP<sup>6</sup> Carey and Whelton highlight the Japan Ambulatory Blood Pressure Monitoring Prospective (JAMP) study,<sup>7</sup> which investigated the association between night-time BP patterns and cardiovascular events; reverse-dipping was again found to be significantly associated with higher cardiovascular disease (CVD) risk.

The prevalence of reverse-dipping has been reported to be between 3% and 39%,<sup>1</sup> depending on study setting and participant characteristics, especially with respect to co-morbidities of interest (e.g. sleep apnoea syndrome, diabetes mellitus and known essential hypertension).

We recently published a retrospective analysis of 1.7 million BP measurements for in-hospital patients, which showed reverse-dipping was the dominant phenotype in this patient group.<sup>8</sup> The analysis of nocturnal SBP presented in this paper is timely and important, given that formal assessment of BP via Ambulatory Blood Pressure Monitoring (ABPM) in primary care has become less frequent since the COVID-19 pandemic, due to challenges accessing and delivering healthcare. Home BP monitoring has provided a partial solution to these challenges<sup>9</sup> and NHS England and NHS Improvement are now distributing home BP monitors to patients to record their day-time BP as part of the *Blood Pressure @home programme*.<sup>10</sup>

In this paper, we estimate the *relative prevalence* of the three SBP phenotypes (dipper, non-dipper and reverse-dipper) in two patient cohorts of the same age group; investigate the association of the reverse-dipping phenotype with average *day-time* SBP; and discuss the implications of this association on screening for hypertension using day-time measurements in General Practice.

## 2. Datasets:

### 2a. In-hospital blood pressure dataset:

We collected BP measurements from patients admitted between March 2014 and April 2018 to four acute hospitals in Oxford University Hospitals NHS Foundation Trust, UK. The study was approved by the Oxfordshire Research Ethics Committee (reference: 16/SC/0264), with Confidentiality Advisory Group approval to process patient data without consent (reference: 16/CAG/0066).

We analysed the SBP of patients aged  $\geq 18$  years from all wards, excluding maternity and intensive care units. We included all patients with at least 3 recorded BP measurements, with at least one recorded during night-time and at least one recorded during day-time, and with 2 of these observations being at least 24 hours apart. This methodology has been described in two earlier papers.<sup>8,11</sup> Using recorded ICD-10 codes for the eligible patients, we investigated the prevalence of cardiometabolic comorbidity (Hypercholesterolaemia, Coronary Heart Disease, Coronary Artery Bypass Graft, Heart Failure, Transient Ischaemic Attack, Peripheral Vascular Disease, Atrial Fibrillation, Chronic Kidney Disease, and Diabetes) among the cohort.

## **2b. Community ABPM dataset:**

The BP-Eth study was an observational study conducted between June 2010 and December 2012 with patients registered at one of 28 General Practices in the UK.<sup>12,13</sup> Patients were aged 40-75 years with and without diagnosed hypertension. Ethical approval was granted by the Black Country Research Ethics Committee, West Midlands (Ref 09/H1202/114).

The BP-Eth protocol involved comparing 24-hour ABPM and GP-clinic BP measurements to investigate the association between 'white coat hypertension' and ethnicity. BP was measured every 30 minutes during the day and hourly during the night using Spacelabs 90217-1Q monitors.<sup>13</sup> We restricted our analyses to those patients who had at least 50% of day-time (9 of 18) and night-time (4 of 8) measurements available (585 patients met those criteria). We investigated the prevalence of the same cardiometabolic comorbidities searched for among the in-hospital blood pressure dataset.

## **3. Methods:**

To enable comparisons between the two datasets, we limited our analysis of the in-patient cohort to patients aged 40-75 years.

### ***24-hour BP profile analysis***

To derive the 24-hour SBP profiles for the two datasets, we divide the 24 hours from midnight to 23:59 into 24 one-hour bands. We define the night-time period to be from the start of the 23:00-23:59 one-hour band up to the end of the 06:00-06:59 one-hour band. We define the day-time period to be from the start of the 09:00-09:59 one-hour band up to the end of the 17:00-17:59 one-hour band, as this is the time period during which day-time BP measurements are most likely to be made in General Practice.

The selection of these night-time and day-time periods creates a two-hour gap between the end of night-time and the start of day-time, such that data from the period during which there is greatest uncertainty as to whether a BP measurement belongs to the night or day are omitted. Similarly, the night-time period is not deemed to start until 23:00 to ensure that the BP measurements used to compute night-time averages are most likely to belong to the sleep part of the sleep-wake cycle. With this clear separation between night-time and day-time periods, we aim to establish whether the extra information available from night-time measurements obtained through ABPM justifies its extra cost and difficulty, compared to standard day-time measurements in clinic.

For each patient, BP data are assigned to one of the 24 one-hour bands and their average SBP for each one-hour band is computed from all data within that band. For patients in the in-hospital dataset, this means averaging data, for each band, from different days; each patient therefore contributes one 24-hour "profile" regardless of their length of hospital admission. For the ABPM dataset, two measurements taken 30 minutes apart are averaged to derive the BP value in each day-time one-hour band.

For both datasets, the SBP values in each one-hour band are used to compute the night-time and day-time average values for that patient, enabling their 24-hour SBP profile to be assigned to one of the following phenotypes:

1. Dipper: Night-time average systolic BP < 90% of day-time average systolic BP
2. Non-dipper: Night-time average systolic BP  $\geq$  90% and <100% of day-time average systolic BP
3. Reverse-dipper: Night-time average systolic BP  $\geq$  100% of day-time average systolic BP

In this paper, we also introduce the ‘extreme reverse-dipper’ as a subtype of the reverse-dipper, defined as:

- 3a. Extreme reverse-dipper: Night-time average systolic BP  $\geq$  110% of day-time average systolic BP.

24-hour SBP profiles characterising each phenotype, for each of the two datasets, are obtained by aggregating the 24-hour profiles for all patients in the dataset with that phenotype.

Sex differences in BP trajectories over the life course have recently been highlighted,<sup>14</sup> and so data analyses are repeated separately for men and women.

## 4. Results

### 4.1. Analysis of in-hospital data:

There were 21,716 patients aged 40-75 years who met our eligibility criteria, during the study period. 7,220 (33.2%) had a preceding diagnosis of hypertension. The mean age was 60.6 (SD 9.9) and 51.1% were male.

Table 1 reports the average number of BP measurements available for the 21,716 participants eligible for inclusion in the analysis.

The relative prevalence of the four SBP phenotypes for hospital patients in the 40-75 age group is given in Table 2, alongside the average day, night and day-night difference in SBP. The 24-hour SBP profiles for this age group are presented on a single plot, for comparison purposes, in Figure 1. Table 2, and the 24-hour SBP profiles in Figure 1, show that the average day-time SBP of dippers is higher than the day-time SBP of non-dippers and reverse-dippers. For reverse-dippers the difference between average day-time and night-time SBP is +8.0 mmHg. Extreme reverse-dippers (a sub-set of reverse-dippers, representing 11.9% of the 40-75 age group) have the lowest day-time SBP average (122.1 mmHg), but their night-time average SBP is 17.3 mmHg higher (139.4 mmHg). We found no evidence of a difference between men and women. Table 2 also reports the prevalence of cardiometabolic comorbidity among in-hospital patients for each of the four SBP phenotypes, to help consider the cardiovascular risk of patients in each of these groups.

### 4.2 Analysis of Community ABPM data:

770 primary care patients contributed ABPM data to this analysis. 481 (62.5%) had a preceding diagnosis of hypertension. The mean age was 58.6 (SD 9.6) and 48.6% were male.

Table 3 reports the average number of BP measurements available for the 585 participants eligible for inclusion in the analysis.

Table 4 shows the numbers and percentages of these 585 patients in the ABPM dataset associated with the four SBP phenotypes, alongside their average day-time and night-time SBPs.

The prevalence of reverse-dipping was 10.8% in this community cohort. This demonstrates that this phenotype does exist in the community, as shown by the 24-hour SBP plots for the four phenotypes in Figure 2. Figure 2 shows again that dippers have a higher day-time average SBP than non-dippers and reverse-dippers. For reverse-dippers and extreme reverse-dippers, the average night-time SBP is 8.5 mmHg and 18.8 mmHg above the average day-time SBP, respectively.

## 5. Discussion

### Summary

Analysis of the first dataset considered in this paper shows that 49% of in-hospital patients aged 40-75 were reverse-dippers. Evidence of reverse-dipping was also present in 11% of subjects in a smaller community dataset of ABPM measurements. Participants in the hospital cohort had a median of 27 blood pressure measurements available for assessment of their 24-hour SBP phenotype whilst participants in the community ABPM cohort had a median of 28 measurements. The interquartile range varied markedly between the two cohorts, being 34 for the in-hospital cohort and 6 for the community cohort.

Figures 1 and 2 show that the SBP of dippers decreases during the night ("negative" half-cycle) before it increases from the early morning onwards ("positive" half-cycle). With reverse dippers (red line in Figure 1), the order of the two half-cycles in the SBP profile is reversed: the night-time rise (positive half-cycle) is followed by the negative half-cycle during the day, and so with this phenotype SBP is *lowest during the day-time period*. As with reverse dippers, non-dippers also have lower day-time SBP and much higher night-time SBP than the dipper phenotype.

For the community cohort, the average *day-time* SBP of dippers (blue line in Figure 2) is 4.4 mmHg higher than that of non-dippers (black line in Figure 2), and 6.8 mmHg higher than that of reverse dippers (red line in Figure 2). For the in-hospital cohort, the differences are 4.4 mmHg and 6.5 mmHg, respectively.

The prevalence of recorded cardiometabolic comorbidity was markedly higher in the community cohort than the in-hospital cohort. There are several potential contributing reasons for this observation; firstly, the community cohort included a much higher prevalence of patients with known hypertension and thus such patients are more likely to be investigated for, diagnosed with and coded for, end-stage disease from hypertension, either as part of primary prevention or when receiving a diagnostic work-up for an acute presentation. Secondly, the two cohorts may be fundamentally different in terms of cardiometabolic health status. Importantly, the same pattern is seen in both cohorts, with the prevalence of cardiometabolic comorbidity rising across the spectrum of phenotypes, from dipping to extreme reverse dipping. This highlights the higher cardiovascular risk status of reverse dippers and extreme reverse dipper patients.

### Strengths and limitations

A very large dataset was used for the analysis of in-hospital BP (21,716 patients). The study was inclusive of adult patients aged between 40 and 75 presenting with all medical problems, only excluding those admitted to maternity or intensive care units. Whilst much smaller, the size of the community dataset was also a strength, with 585 participants contributing ABPM data for analysis.

We observed a markedly different prevalence of the reverse-dipping phenotype between the hospital in-patient and community cohorts. There are several potential factors that may contribute to this and



may limit comparisons between the two datasets. Firstly, the prevalence of diagnosed hypertension was much higher in the community cohort than the in-hospital cohort (62.5% versus 33.2%, respectively). Additionally, variation in the quality and number of blood pressure measurements contributing to the 24-hour SBP analysis may have an impact on the comparability of our results between the in-hospital community cohorts; whilst the median number of BP measurements per participant for the two cohorts was very similar (27 in hospital versus 28 in the community), the interquartile range was much higher in the hospital cohort, indicating greater variability in the number of SBP measurements available.

Our aim for this study was not to compare 'office' or in-hospital BP with community ABPM within individuals. Rather, we sought to analyse data for two cohorts on a population level, to determine whether the same phenotypes exist within the hospital and community cohorts. The prevalence of the non-dipping and reverse-dipping SBP phenotypes in both cohorts highlights the importance of measuring blood pressure over 24 hours to detect and diagnose hypertension.

We did not find any significant differences between the average SBPs of men and women in the day-time or the night-time, but this may be because of the choice of age group (40-75). In our previous work,<sup>11</sup> we had shown that women below the age of 60 had lower SBPs than men, but the opposite was true above the age of 60. These two phenomena would then average out in a combined 40-75 age group.

This study used systolic BP only to compute the 24-hour BP phenotypes of the included participants, conforming to common practice in this field.<sup>17-19</sup> Future work could include an analysis of whether 24-hour diastolic blood pressure profiles provide independent information.

### **Comparison with existing literature**

The review by Cuspidi et al. gives a prevalence for reverse dipping between 3% and 39%.<sup>1</sup> Reverse-dipping is primarily associated with OSA and arousal.<sup>10</sup> Measuring vital signs at night in hospital is likely to cause an arousal to wakefulness, and so the 49% prevalence in our in-hospital cohort is very likely to be an upper bound. The prevalence of non-dipping reported in this manuscript for the hospital cohort should therefore be interpreted within this context.

A study of hypertensive patients in a primary care setting in Europe<sup>5</sup> reported a similar prevalence of reverse dipping (12.1%) to that found in our community ABPM dataset. In a sub-study of 374 patients in Belgium, of whom 32.6% had been prescribed anti-hypertensives, reverse dipping was observed in 14.4% patients.<sup>15</sup> The figure of 11% for reverse-dippers in our community cohort is in line with these data, but is probably a lower bound.

Previous studies have reported poor reproducibility of the dipper blood pressure phenotype within individuals; a meta-analysis of 14 studies revealed that up to 32% of participants were inconsistent dippers (i.e. dippers became non-dippers or vice versa) on repeat ABPM.<sup>16</sup> It is possible therefore that if the study were repeated, some patients may be categorised differently; however, this would be unlikely to affect the proportion of patients categorised into each of the four phenotypes, as a further meta-analysis of 11 relevant studies revealed no difference in the rate of systolic nocturnal BP dipping between a first and second ABPM.<sup>16</sup> Furthermore, for our hospital cohort, the 24-hour BP profile was computed using SBP measurements taken throughout their hospital admission, and therefore patients in this cohort have a blood pressure profile consisting of measurements taken from multiple days; their 24-hour SBP profile represents a longitudinal, averaged picture.

### **Implications for clinical practice**

BP is measured in General Practice during day-time hours when the *BP of reverse-dippers and non-dippers is lowest*, thus placing them at risk of undiagnosed, or masked hypertension. Clinicians measuring their BP will not know that the population *average* night-time SBP of reverse dippers is 8 mmHg higher than their average day-time SBP. Conversely, dippers experience their highest SBP during the time when it is measured in General Practice and hence are more likely to be diagnosed.

European and International guidelines for the management of hypertension include diagnostic thresholds for night-time hypertension.<sup>21,22</sup> However, when ABPM is performed in the UK, NICE recommend using only day-time BP measurements to assess for hypertension.<sup>20</sup> Thus, not only is hypertension likely to go undetected in reverse-dippers when assessed with day-time clinic BP measurements, their elevated nocturnal measurements on ABPM when it is performed, are likely to be disregarded. Indeed, the average night-time SBP of reverse dippers in our hospital and community cohorts were 132.1 mmHg and 137.7 mmHg, respectively. This was 18.0 mmHg and 24.9 mmHg higher than the average night-time SBP of dippers in each respective cohort. This is a clinically important difference when considering cardiovascular risk and need to treat. In most cases, when a clinical decision regarding whether to treat someone for hypertension is made, consideration of the 24-hour SBP phenotype of dipper or non-dipper is less likely to influence the decision than knowledge of the average day, night or 24-hour BP values. This study has demonstrated that 24-hour SBP should be assessed in order to detect those who are non-dippers or reverse dippers with isolated nocturnal hypertension but with normal day-time clinic BP. Paradoxically, it is those individuals with the dipping SBP phenotype who have their highest SBP during the day-time period, and are therefore more likely to be diagnosed in the clinic as being hypertensive. It should also be noted that people from black and Asian populations may be differentially affected by this issue; the non-dipping phenotype is more prevalent among black<sup>23</sup> and Asian<sup>3</sup> populations than white populations.

In most cases, when a clinical decision regarding whether to treat someone for hypertension is made, consideration of the 24-hour SBP phenotype of dipper or non-dipper is less likely to influence the decision than knowledge of the average day, night or 24-hour BP values. This study has demonstrated that in the first instance 24-hour SBP should be assessed in order to detect those who are non-dippers or reverse dippers with isolated nocturnal hypertension but normal day-time clinic BP screening. Paradoxically, it is those individuals with the dipping SBP phenotype who have their highest SBP during the day-time period, and are therefore more likely to be diagnosed in the clinic as being hypertensive.

We showed, in our original analysis of the in-hospital cohort, that peak nocturnal SBP increased after the age of 60,<sup>11</sup> and previous work has shown that reverse dipping increases with age.<sup>4</sup> These findings, together with the evidence presented here, demonstrate that night-time BP recorded via ABPM should form part of the clinical assessment for hypertension in the UK, as is currently recommended in Europe<sup>21</sup> and this is particularly important for those aged  $\geq 60$  years. Furthermore, the prevalence of reverse-dipping in hospital patients, even if it is an upper bound, indicates that those without a previous diagnosis of hypertension could benefit from automatic screening of their in-hospital 24-hour SBP to identify who should receive post-discharge ABPM in the community.<sup>24</sup> If the delivery of ABPM at scale is too great a burden for primary care, it is time to investigate alternative technologies for 24-hour BP monitoring<sup>7,25,26</sup> in the home.

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## Conflicts of interest

AJF is Director of the NIHR Health Technology Assessment Programme. PW and LT report significant grants from the National Institute of Health Research (NIHR), UK and the NIHR Biomedical Research Centre, Oxford, during the conduct of the study. PW and LT report modest grants and personal fees from Sensyne Health, outside the submitted work. PW was Chief Medical Officer for Sensyne Health. LT works part-time for Sensyne Health and holds shares in the company. RM has received BP monitors from Omron Healthcare for research purposes and is working with them on a telemonitoring system.

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	<b>Whole Cohort</b>	<b>Men</b>	<b>Women</b>
Number of Patients	21,739	11,111	10,628
No. Measurements, Mean (SD)	39.6 (47.3)	40.8 (45.8)	38.3 (48.9)
No. Measurements, Median (IQR)	26 (31)	27 (32)	25 (29)
Mean 24h SBP, Mean (SD)	126.3 (15.4)	127.5 (15.0)	125.1 (15.7)
Mean 24h SBP, Median (IQR)	125.1 (20.3)	126.3 (19.6)	123.6 (20.8)

### Tables and legends

**Table 1.** Average number of blood pressure measurements, per-participant, contributing to the analysis of in-hospital 24-hour blood pressure phenotypes.

Phenotype		Dippers	Non-dippers	Reverse-dippers	Extreme reverse-dippers*
Whole cohort	Percentage in each phenotype (%)	10.5	40.6	48.9	11.9
	Day-time SBP (mmHg)	130.6	126.2	124.1	122.1
	Night-time SBP (mmHg)	114.1	121.5	132.1	139.4
	Day-night difference (mmHg)	-16.5	-4.7	+8.0	+17.3
	24h mean SBP (mmHg)	124.8	125.0	127.7	129.2
	Prevalence of cardiometabolic comorbidity (%)	22.4	23.6	35.9	42.3
Men	Day-time SBP (mmHg)	132.5	127.6	124.7	122.1
	Night-time SBP (mmHg)	115.9	123.1	132.8	139.6
	Day-night difference (mmHg)	-16.6	-4.5	+8.1	+17.5
	24h mean SBP (mmHg)	126.6	126.6	128.4	129.3
	Prevalence of cardiometabolic comorbidity (%)	27.2	26.7	40.2	47.2
Women	Day-time SBP (mmHg)	129.0	124.6	123.5	122.0
	Night-time SBP (mmHg)	112.6	119.8	131.2	139.3
	Day-night difference (mmHg)	-16.4	-4.8	+7.7	+17.3
	24h mean SBP (mmHg)	123.2	123.4	127.0	129.1
	Prevalence of cardiometabolic comorbidity (%)	18.2	20.7	31.7	38.0

**Table 2.** Relative prevalence of each of the four systolic blood pressure phenotypes observed in hospital patients aged 40-75, alongside average SBP for night and day and the day-night difference in each of the four SBP phenotypes and the prevalence of cardiometabolic comorbidity in each of the phenotypes. \*Extreme reverse-dippers are a sub-set of the reverse-dipper phenotype.

	<b>Whole Cohort</b>	<b>Men</b>	<b>Women</b>
Number of Patients	585	288	297
No. Measurements, Mean (SD)	26.9 (4.2)	27.2 (4.0)	26.5 (4.3)
No. Measurements, Median (IQR)	28 (6)	28 (5)	27 (6)
Mean 24h SBP, Mean (SD)	129.5 (14.3)	130.4 (13.2)	128.6 (15.3)
Mean 24h SBP, Median (IQR)	128.6 (17.2)	129.6 (14.4)	126.7 (18.7)

**Table 3.** Average number of blood pressure measurements, per-participant, contributing to the analysis of community 24-hour blood pressure phenotypes.

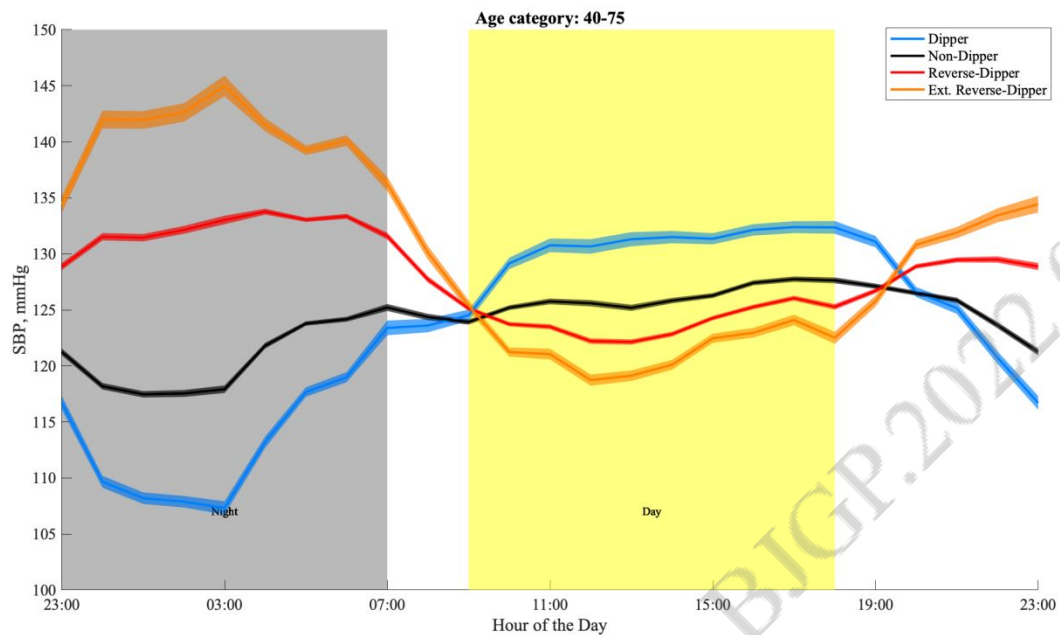
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Phenotype		Dippers	Non-dippers	Reverse-dippers	Extreme reverse-dippers*
Whole Cohort	Percentage in each phenotype (%)	56.9	32.3	10.8	3.1
	Day-time SBP (mmHg)	136.0	131.6	129.2	122.6
	Night-time SBP (mmHg)	112.8	123.9	137.7	141.4
	Day-night difference (mmHg)	-23.2	-7.7	+8.5	+18.8
	24h mean SBP (mmHg)	128.6	129.8	133.3	130.5
	Prevalence of cardiometabolic comorbidity (%)	47.7	58.2	63.5	66.7
Men	Percentage in each phenotype (%)	56.6	31.6	11.8	4.2
	Day-time SBP (mmHg)	138.1	131.3	129.3	121.7
	Night-time SBP (mmHg)	114.0	123.4	137.6	138.5
	Day-night difference (mmHg)	-24.1	-7.9	+8.3	+16.8
	24h mean SBP (mmHg)	130.5	129.3	132.9	128.2
	Prevalence of cardiometabolic comorbidity (%)	54.6	60.4	64.7	58.3
Women	Percentage in each phenotype (%)	57.2	33.0	9.8	2.0
	Day-time SBP (mmHg)	134.1	131.9	129.2	124.3
	Night-time SBP (mmHg)	111.6	124.4	137.7	147.3
	Day-night difference (mmHg)	-22.5	-7.5	+8.5	+23.0
	24h mean SBP (mmHg)	126.8	130.2	133.9	135.1
	Prevalence of cardiometabolic comorbidity (%)	41.2	56.1	62.1	83.3

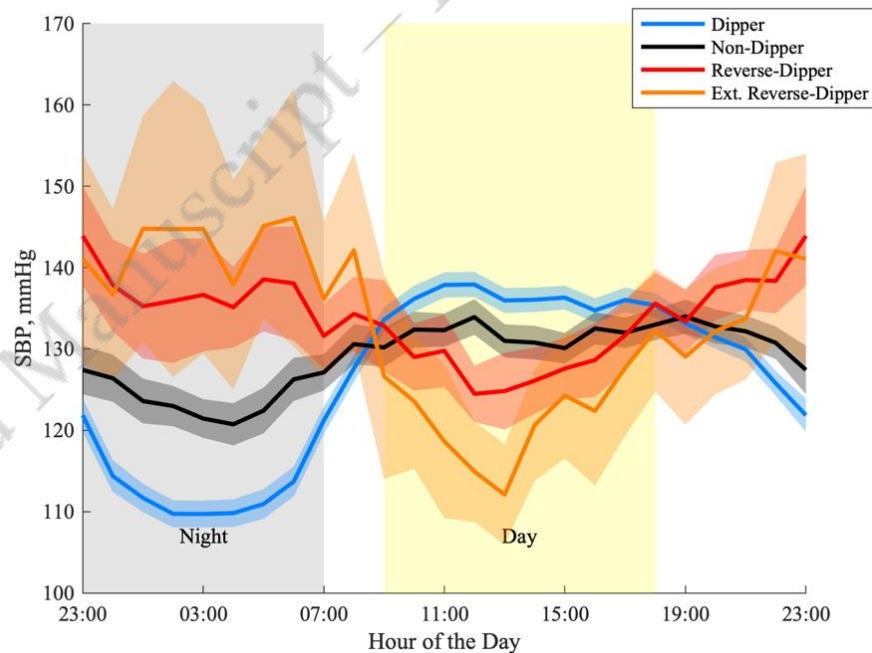
**Table 4.** Relative prevalence of each of the four systolic blood pressure phenotypes observed for community patients, alongside average SBP for night and day and the day-night-time difference in each of the four SBP phenotypes and the prevalence of cardiometabolic comorbidity in each of the phenotypes. \*Extreme reverse-dippers are a sub-set of the reverse-dipper phenotype.



## Figures and legends



**Figure 1.** 24-hour systolic blood pressure profiles for each of the four SBP phenotypes observed for hospital patients aged 40-75. The width of each coloured line is proportional to the variance of the data for that data point (one data point for each one-hour bin).



**Figure 2.** 24-hour systolic blood pressure profiles for each of the four SBP phenotypes observed for community patients. The width of each coloured line is proportional to the variance of the data for that data point (one data point for each one-hour bin).