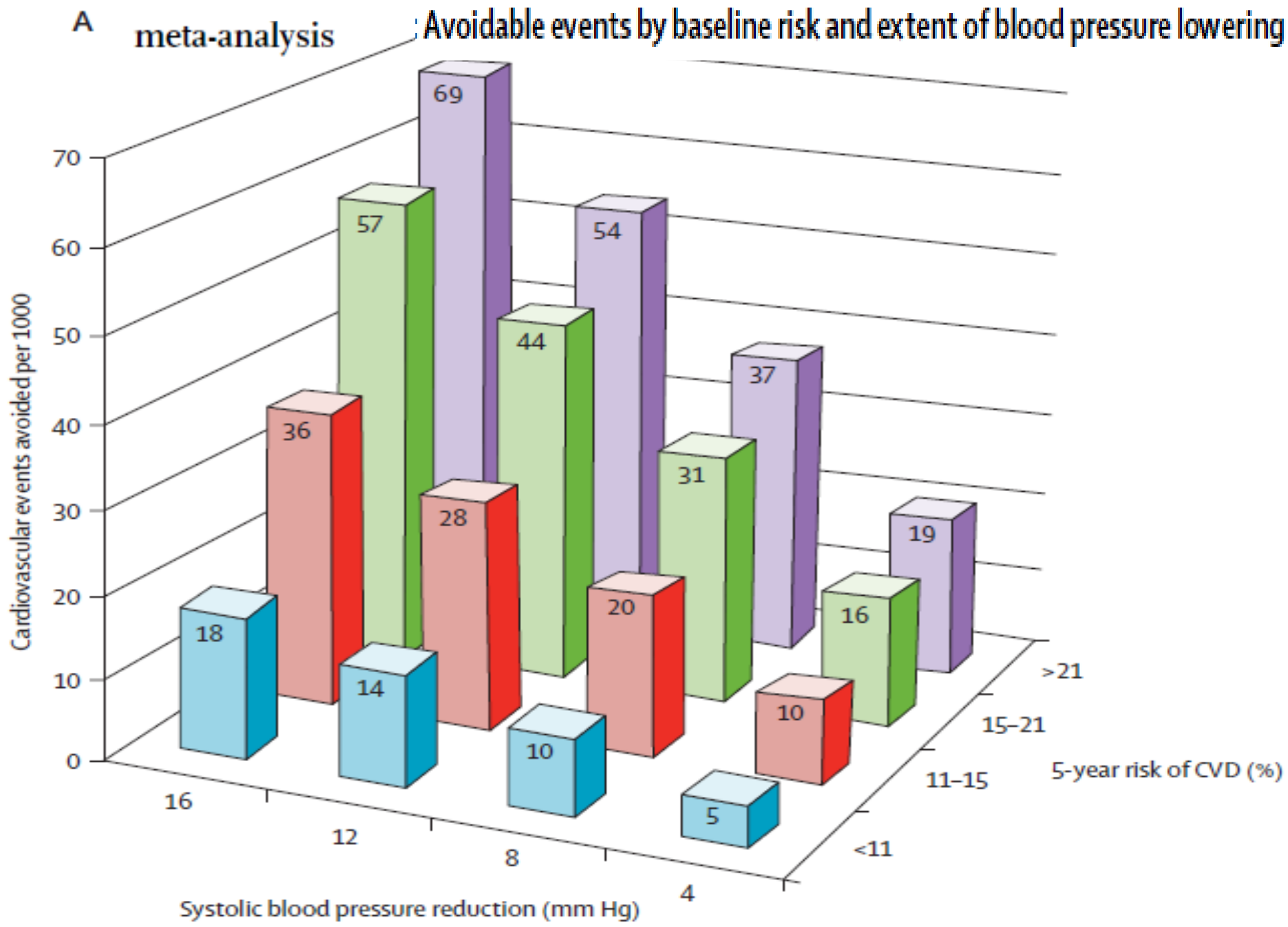
Le bon usage de la **Mesure Ambulatoire de la Pression Artérielle**, focus sur la **Chronothérapie**

Prof JM Krzesinski CHU Liège - ULiège

Pas de conflit d'intérêt pour cet exposé

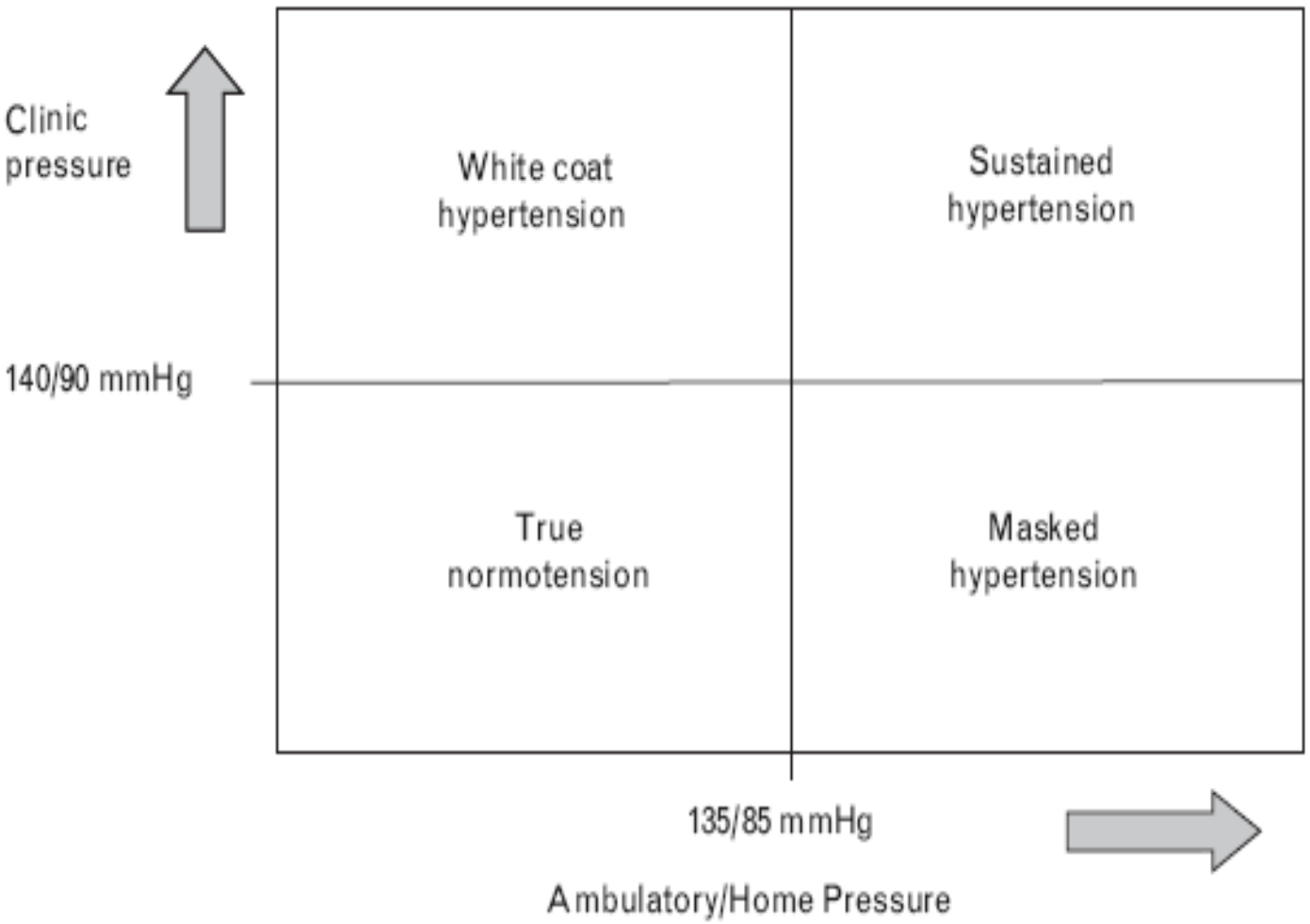


The Blood Pressure Lowering Treatment Trialists' Collaboration*

Lancet 2014; 384: 591–98

Volhard lecture: masked hypertension Pickering *et al.*

JHTA2008



Questions face à une augmentation de PA mesurée au cabinet de consultation

- Mon patient est-il réellement hypertendu?
- Répétition des mesures au cabinet mais risque de rater l'HTA blouse blanche et l'HTA masquée!
- Nécessité devant toute élévation de PA de confirmer par des mesures en dehors de la consultation!

L'automesure à domicile
But PA <135/85 mmHg

Idéal:
- manchette au bras.
- appareil validé.
- contrôle avec le médecin.

Avantage:
-plus prédictive du risque d'événements cv
et de la mortalité cv que la PA clinique *

Limite:
-pas d' information sur PA de nuit.

Fréquence des mesures
- après 5 min. de repos/30 min. sans tabac ni café
- 2 mesures (mat et soir) / jour pendant 7 jours.
- ne pas tenir compte des mesures du 1er jour.
- suivi à long terme: 1 à 2 mesures/semaine ou 1 sem./mois

* Ward A. et al. Meta-analysis of prospective studies. J Hypertens 2012;30:449-456

Free Radic Biol Med. 2018 May 01; 119: 108–114. doi:10.1016/j.freeradbiomed.2017.11.024.

Circadian Clock-Mediated Regulation of Blood Pressure

Lauren G. Douma[1,2] and **Michelle L. Gumz**[1,2,*]

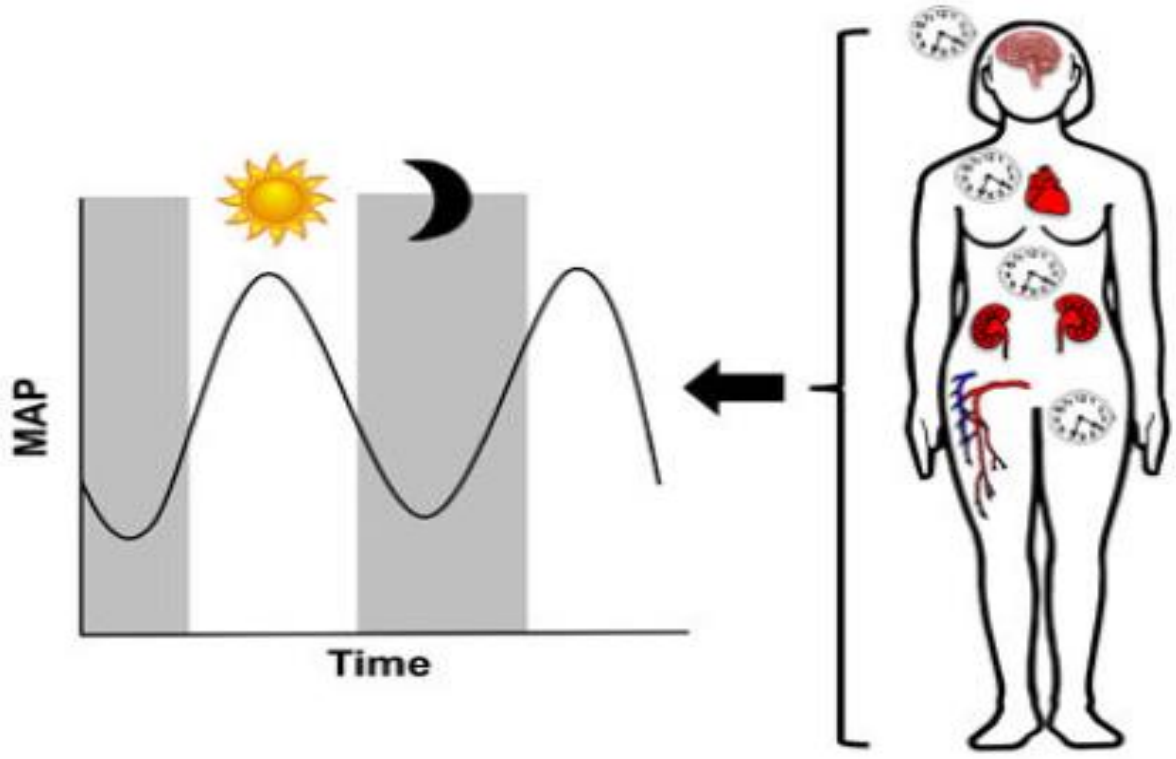
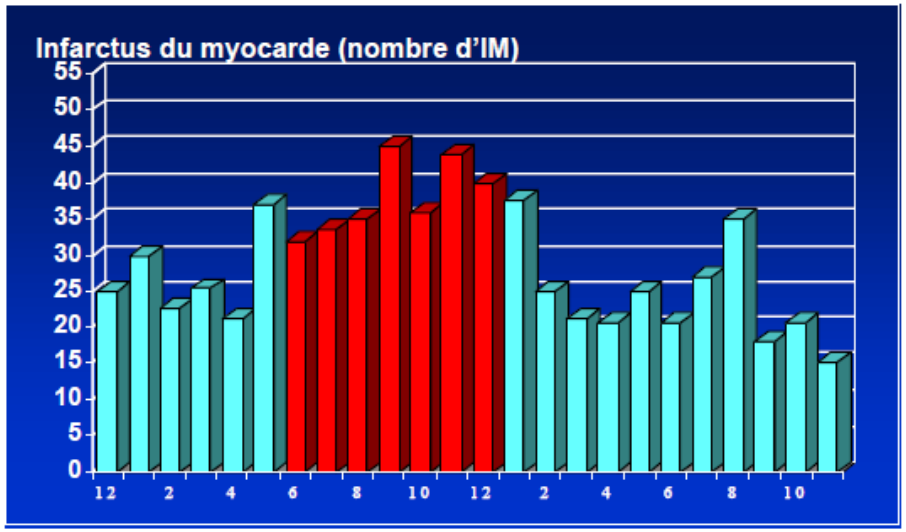


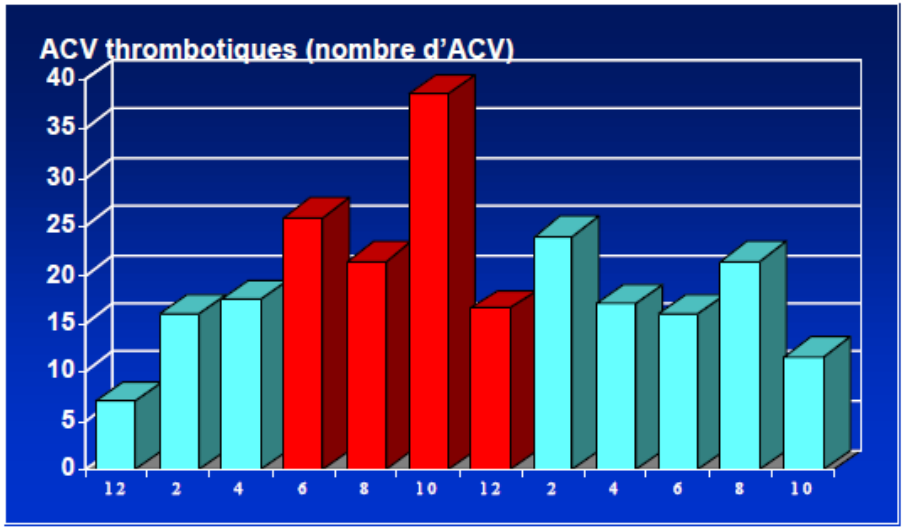
Figure 1. Molecular circadian clocks throughout the body contribute to the circadian rhythm of blood pressure

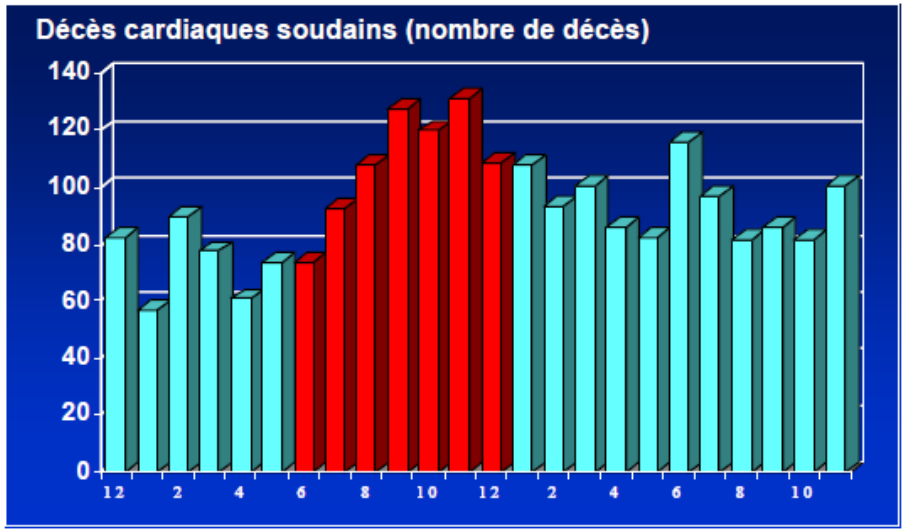
Studies with rodents and humans suggest that clock components within the kidneys, brain, nervous system, heart, and vasculature all contribute to the regulation of the BP circadian cycle. The molecular circadian clock within these tissues regulates the physiological functions that contribute to overall BP regulation. BP has a 24-hour cycle, with a peak in BP during the day and a 10-20% dip in BP at night. Dysregulation of the BP circadian rhythm can have profound effects, including a greater risk of stroke and cardiovascular disease.

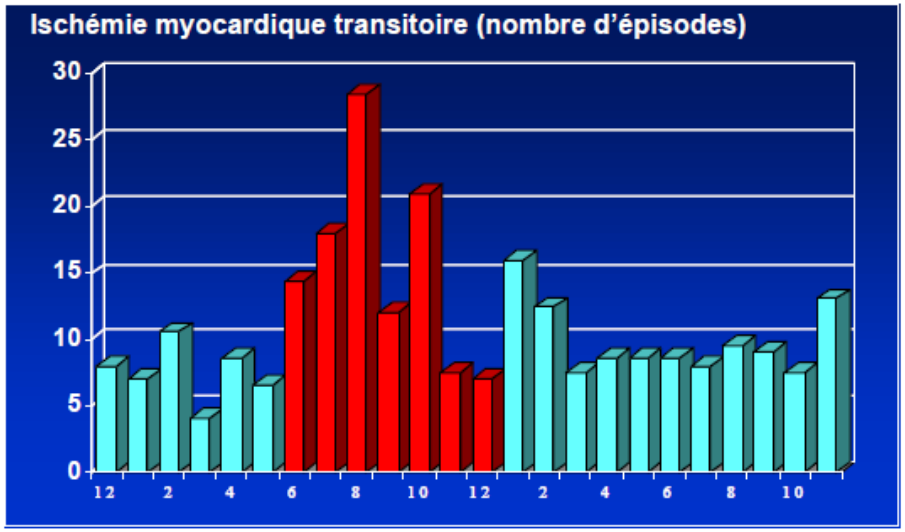
Maîtrise de la tension artérielle durant 24 h

Variations circadiennes pour les maladies cardiovasculaires aiguës



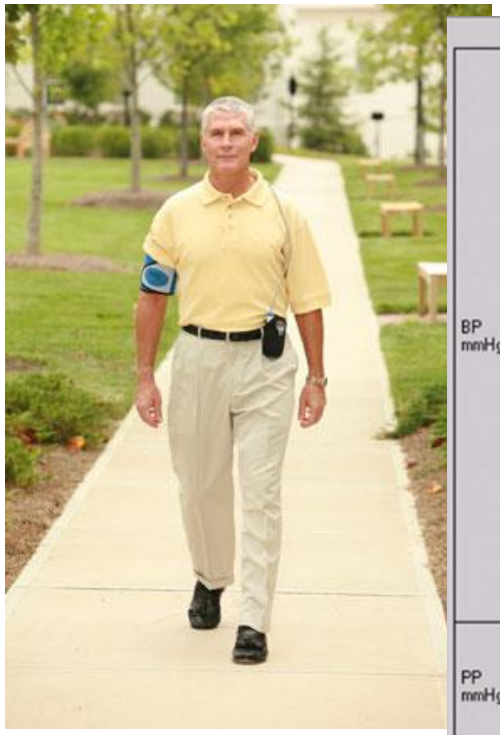


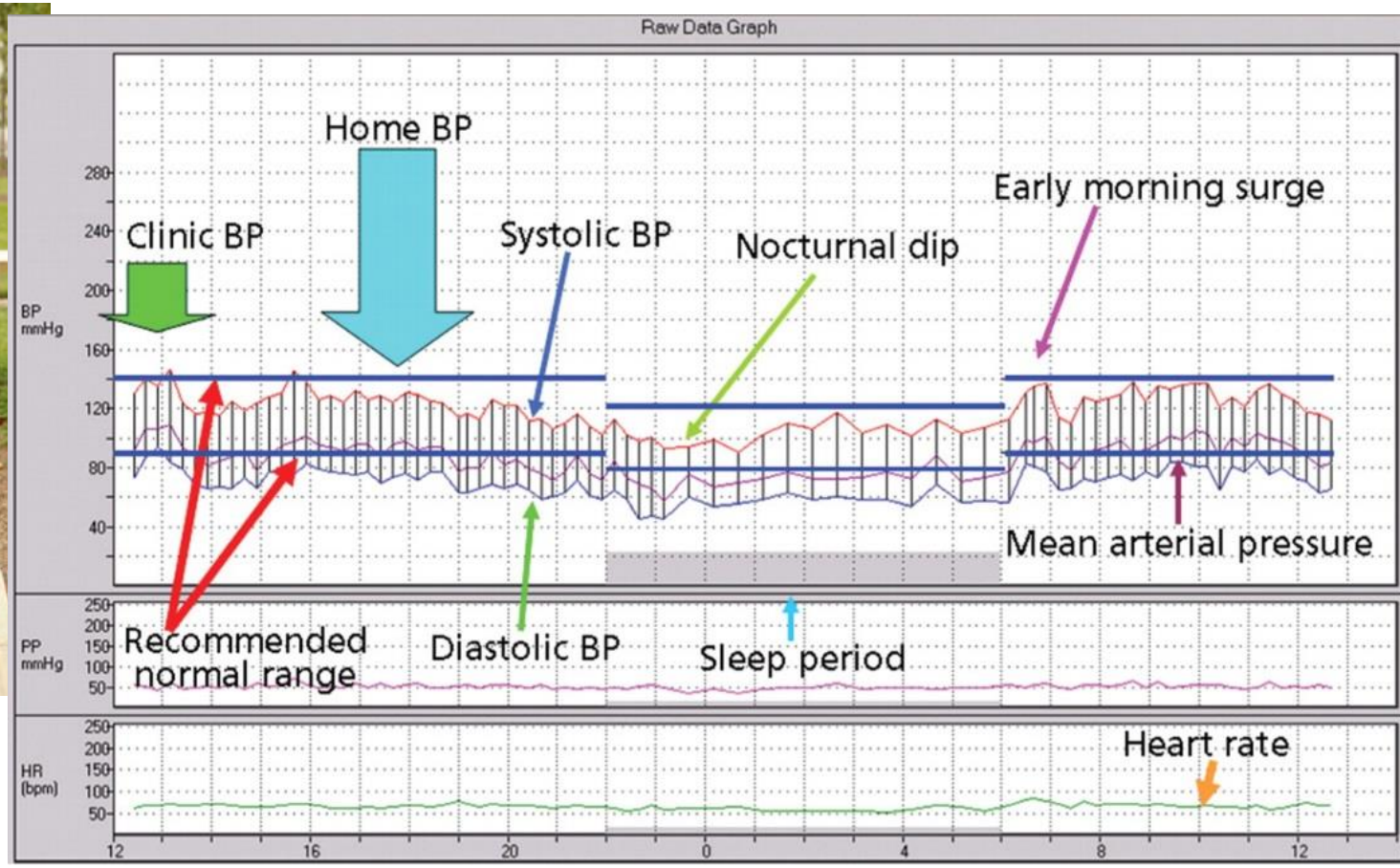




Muller J ; *Circulation* 1989 : Vol 79, 4, 733-43

Monitoring Ambulatoire de Pression Artérielle de 24h





Journal of Hypertension 2014, 32:1359–1366

<u>Avantages</u>:

- Observation d'une HTA nocturne
- Observation de la chute de PA la nuit (dipping)
- Observation de la montée de PA au réveil

Relationship between Clinic and Ambulatory Blood-Pressure Measurements and Mortality

J.R. Banegas, L.M. Ruilope, A. de la Sierra, E. Vinyoles, M. Gorostidi, J.J. de la Cruz, G. Ruiz-Hurtado, J. Segura, F. Rodríguez-Artalejo, and B. Williams

63910 patients, 58 ans
4,7 ans de FU

1. MAPA meilleur prédicteur du risque de mortalité que la PA au cabinet.
2. HTA masquée plus dangereuse que HTA identifiée au cabinet de consultation.
3. PA de nuit apporte un plus dans le risque!

N Engl J Med 2018;378:1509-20.

Table 2. Association of Clinic and Ambulatory Blood Pressure with All-Cause and Cardiovascular Mortality in Cox Regression Models.*

Mortality and Blood-Pressure Component	Model 1†		Model 2‡	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
All-cause mortality				
Clinic systolic blood pressure	1.54 (1.52–1.56)	<0.001	1.02 (1.00–1.04)	0.04
Clinic diastolic blood pressure	1.02 (1.00–1.04)	<0.001	0.89 (0.87–0.92)	0.01
24-Hour systolic blood pressure	1.58 (1.56–1.60)	<0.001	1.58 (1.56–1.60)	<0.001
24-Hour diastolic blood pressure	1.56 (1.54–1.58)	<0.001	1.56 (1.54–1.59)	<0.001
Daytime systolic blood pressure	1.57 (1.55–1.60)	<0.001	1.54 (1.52–1.56)	<0.001
Daytime diastolic blood pressure	1.55 (1.53–1.58)	<0.001	1.01 (0.99–1.04)	0.32
Nighttime systolic blood pressure	1.57 (1.55–1.59)	<0.001	1.55 (1.53–1.57)	<0.001
Nighttime diastolic blood pressure	1.56 (1.54–1.59)	<0.001	1.56 (1.54–1.59)	<0.001
Cardiovascular mortality				
Clinic systolic blood pressure	1.54 (1.52–1.56)	<0.001	1.02 (1.00–1.04)	0.08
Clinic diastolic blood pressure	1.02 (0.99–1.04)	0.14	0.89 (0.86–1.00)	0.06
24-Hour systolic blood pressure	1.58 (1.55–1.60)	<0.001	1.58 (1.55–1.60)	<0.001
24-Hour diastolic blood pressure	1.55 (1.53–1.58)	<0.001	1.56 (1.53–1.59)	<0.001
Daytime systolic blood pressure	1.57 (1.55–1.60)	<0.001	1.54 (1.52–1.57)	<0.001
Daytime diastolic blood pressure	1.55 (1.52–1.58)	<0.001	1.01 (0.98–1.04)	0.73
Nighttime systolic blood pressure	1.57 (1.54–1.59)	<0.001	1.55 (1.53–1.57)	<0.001
Nighttime diastolic blood pressure	1.56 (1.53–1.59)	<0.001	1.56 (1.53–1.59)	<0.001

* Of the 63,910 patients included in the analysis, 3808 died from any cause, and 1295 of those died from cardiovascular causes. Hazard ratios

HTA masquée

Table. Prevalence of Masked Hypertension in 3477 Untreated Patients and Masked Uncontrolled Hypertension in 5934 Patients Under Antihypertensive Treatment With Office Blood Pressure <130/<80 mm Hg Using Different Ambulatory Blood Pressure Monitoring-Derived Limits

	Prevalence of Masked Hypertension, n (%) (N=3477)	Prevalence of Masked Uncontrolled Hypertension, n (%) (N=5934)
European Society of Hypertension proposed criteria		
Mean daytime BP ≥ 135 or 85 mm Hg	497 (14.3)	881 (14.8)
Mean 24-h BP ≥ 130 or 80 mm Hg	671 (19.3)	1204 (20.3)
Mean nighttime BP ≥ 120 or 70 mm Hg	977 (28.1)	2149 (36.2)
Any of the above	1147 (33.0)	2349 (39.6)

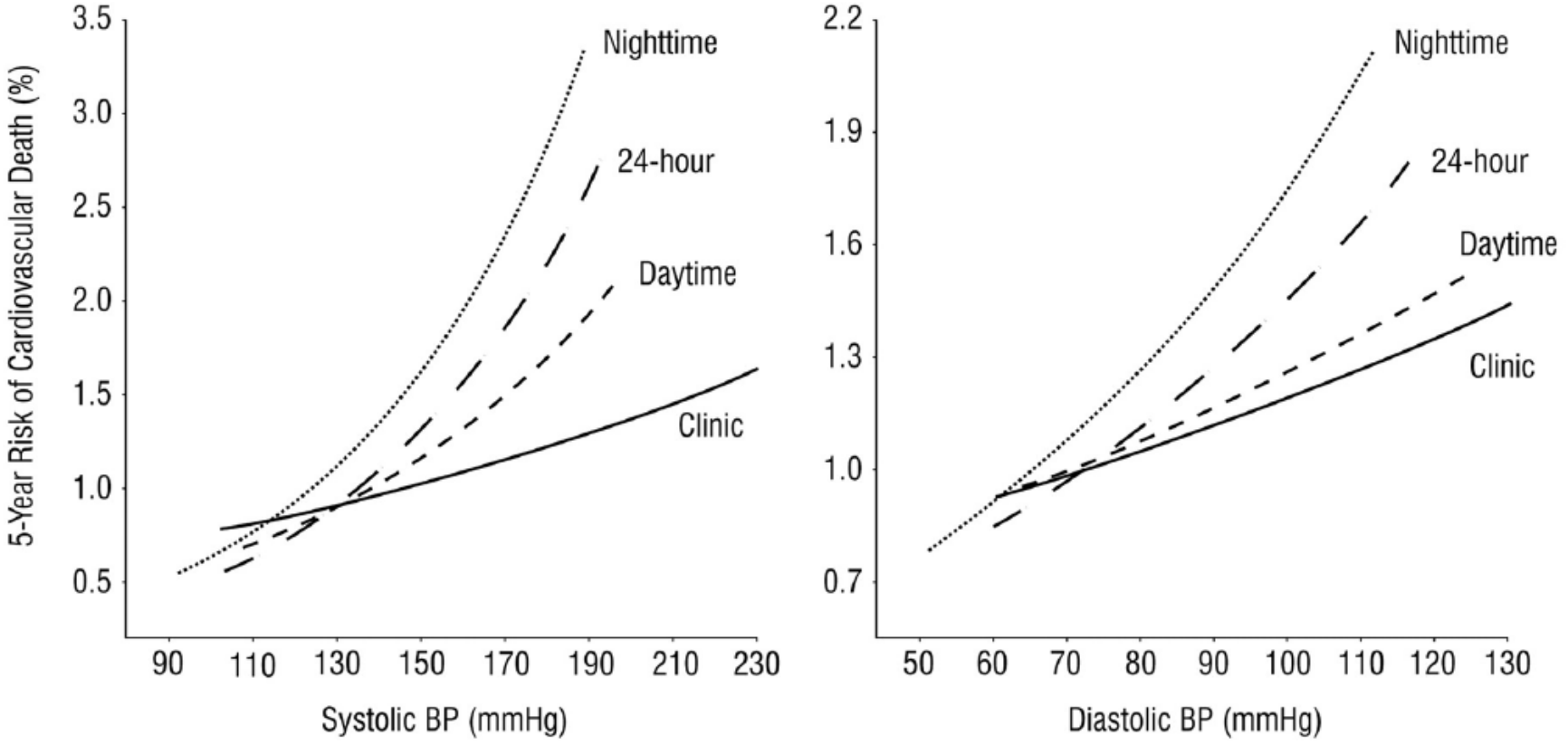
X2

X2,5

HTA masquée surtout la nuit

Circulation. 2018;137:2651–2653.

Supériorité de la valeur prédictive de la TA nocturne sur le plan de la mortalité CV

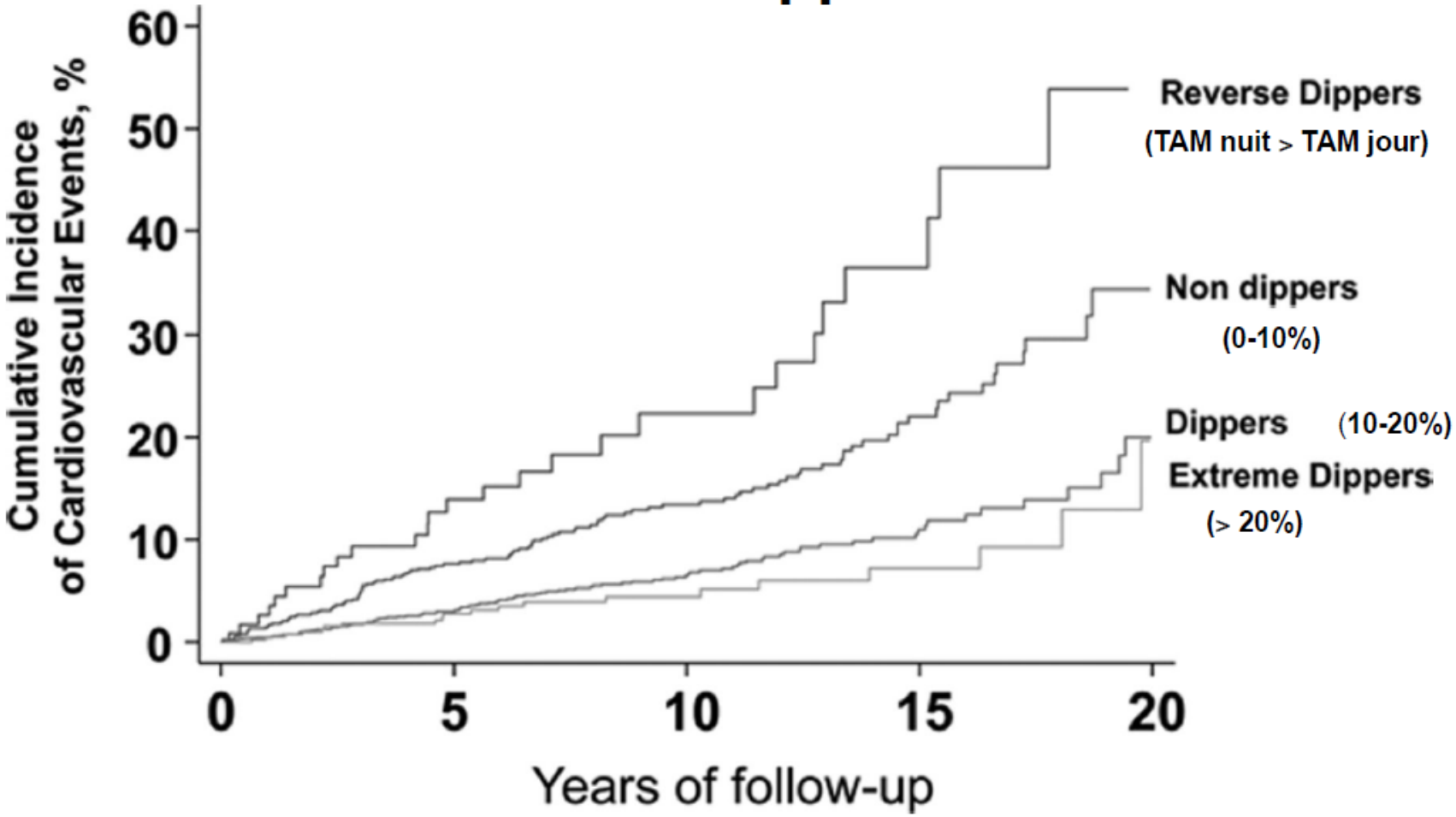


Dolan E et al. Hypertension 2005;46:156-161

5292 HT irlandais
non traités au départ
et suivis 8ans

American Heart Association
Learn and Live

Cumulative incidence of cardiovascular events in dippers, nondippers, reverse dippers, and extreme dippers.



Giuseppe Mancia, and Paolo Verdecchia Circ Res. 2015;116:1034-1045

American Heart Association.

Our analysis is based on a cohort of 3012 subjects with hypertension who were untreated at the time of ABP monitoring.

Causes and consequences of a non-dipping blood pressure profile

Netherlands The Journal of Medicine

A.M. Birkenhäger*, A.H. van den Meiracker

APRIL 2007, VOL. 65, NO. 4

Table 1. *Associated conditions and other influences*

Endocrine conditions	Renal dysfunction	Disturbances of the autonomic nervous system	Miscellaneous
Aldosteronism [5-10]	Chronic kidney damage [1-14]	Pure autonomic failure [57-60]	Salt-sensitive hypertension [42,44,61,62]
Hypercortisolism [63,64]	Renal transplantation [12,18*]	Diabetic neuropathy [65-67]	Pre-eclamptic toxaemia [68]
Pheochromocytoma [69]	Unilateral nephrectomy [53]	Uraemic neuropathy [12]	Malignant hypertension [70]
Acromegaly [71]		Familial amyloidotic polyneuropathy [72]	Cardiac transplantation [73,74*]
Hyperthyroidism [75]		Obstructive sleep apnoea syndrome [76]	Ethnicity [77**]
Hyperparathyroidism [78]			Disturbances in circadian plasma melatonin changes [79]

* Use of immunosuppressive therapy may play a role as well.[80,81] ** People of African ancestry have a higher prevalence of non-dipping than Caucasian

Ambulatory blood pressure monitoring predicts cardiovascular events in treated hypertensive patients – an Anglo-Scandinavian cardiac outcomes trial substudy

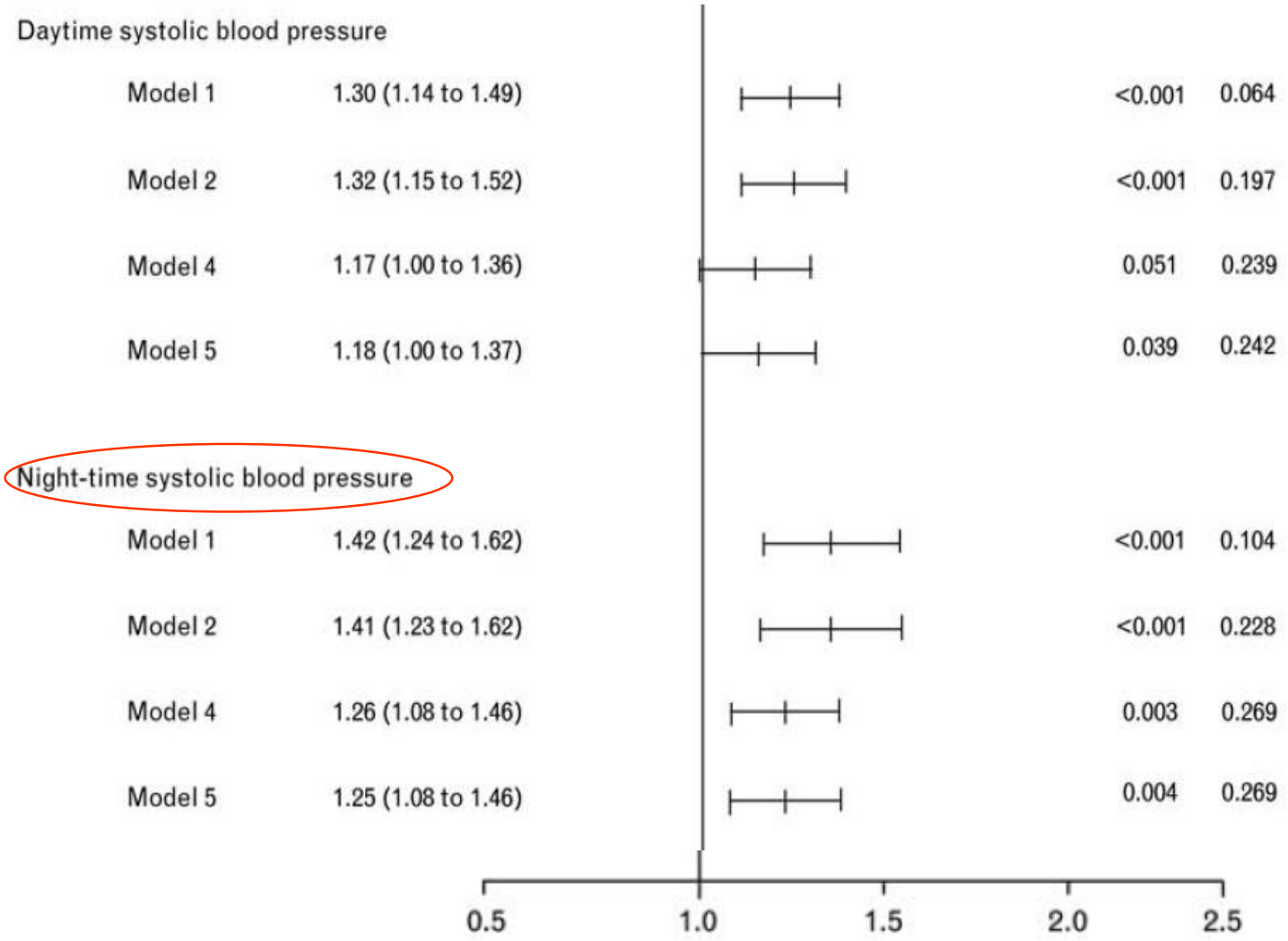
Eamon Dolan[a], Alice V. Stanton[b], Simon Thom[c], Mark Caulfield[d], Neil Atkins[e], Gordon McInnes[f], David Collier[d], Patrick Dicker[b] and Eoin O'Brien[g], on behalf of the ASCOT Investigators*

Background Results of the Anglo-Scandinavian cardiac outcomes trial-blood pressure lowering arm (ASCOT-BPLA) showed significantly lower rates of coronary and stroke events in individuals allocated an amlodipine–perindopril combination drug regimen than in those allocated an atenolol–thiazide combination drug regimen. The aims of the ambulatory blood pressure (ABP) substudy of ASCOT were to examine the impact of the two blood pressure (BP)-lowering regimens on ambulatory pressures, test to what extent the between-treatment differences in cardiovascular outcome could be attributed to differences in ABP and assess whether ABP provides predictive information additional to that of clinic blood pressure (CBP) in treated hypertensive patients.

Journal of Hypertension 2009, 27:876–885

Hazard ratios (HR) for systolic blood pressure variable in relation to total cardiovascular events

ABPM ASCOT



Journal of Hypertension 2009, Vol 27 No 4

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The findings of the ASCOT ABP substudy have clear clinical relevance. Despite the abundance of evidence for the superiority of ABP over clinic BP as a predictor of outcome, current guidelines generally recommend ABP only in selected circumstances. The importance of night-time BP control supports the use of ABP in the follow-up of treated patients. Only ABP allows adjustment of therapy to control night-time BP, which may be crucial in determining outcome.

Journal of Hypertension 2009, Vol 27 No 4

Treatment of Hypertension With Chronotherapy: Is It Time of Drug Administrati[illegible]?

Annals of Pharmacotherapy
2015, Vol. 49(3) 323–334

Awake-BP Reduction

Table 1. Summary of BP and Cardiovascu[illegible]erapy Trials.

Population (n)	Follow-up (Mean)	Baseline 48-Hour BP, Mean	Morning Admin	Bedtime Admin	Percentage Nondipper		Composite CVD Outcome[a] (%)		Reference
					Morning Admin	Bedtime Admin	Morning Admin	Bedtime Admin	
Essential HTN (2201)	5.6 Years	130.6/78.5	9.4/7.2	8.9/6.5	61.6	34.4[b]	17.2	6.3[b]	Hermida et al[6]
Type 2 diabetes (448)	5.4 Years	133.4/74.3	8.3/6.1	9.1/6.3	76.3	49.5[b]	29.3	10.6[b]	Hermida et al[7]
CKD (661)	5.4 Years	134.7/78.4	9.4/6.9	8.1/5.7[b]	71.1	41.0[b]	31.3	10.6[b]	Hermida et al[8]
Resistant HTN (776)	5.4 Years	130/74.7	5.4/4.2	7.3/5.1	74.7	39.2[b]	26	10.6[b]	Ayala et al[22]

Abbreviations: Admin, administration; BP, blood pressure (reported as systolic blood pressure/diastolic blood pressure in mm Hg.); CKD, chronic kidney disease; HTN, hypertension.

[a]Composite CVD outcome: all-cause death, myocardial infarction, angina pectoris, coronary revascularization, heart failure, acute arterial occlusion of the lower extremities, rupture of aortic aneurisms, thrombotic occlusion of the retinal artery, hemorrhagic stroke, ischemic stroke, and transient ischemic attack.

[b]Statistically significant between treatment groups.

Peu d'effet sur PA jour

Treatment of Hypertension With Chronotherapy: Is It Time of Drug Administration?

Annals of Pharmacotherapy
2015, Vol. 49(3) 323–334

Table 1. Summary of BP and Cardiovascular Outco … ls.

Population (n)	Follow-up (Mean)	Baseline 48-Hour BP, Mean	Awake Reduc… Morning Admin	Asleep-BP Reduction: Morning Admin	Asleep-BP Reduction: Bedtime Admin	…ntage …lipper: Bedtime Admin	Composite CVD Outcome[a] (%): Morning Admin	Composite CVD Outcome[a] (%): Bedtime Admin	Reference
Essential HTN (2201)	5.6 Years	130.6/78.5	9.4/7.2	6.6/5.2	11.8[b]/7.9[b]	34.4[b]	17.2	6.3[b]	Hermida et al[6]
Type 2 diabetes (448)	5.4 Years	133.4/74.3	8.3/6.1	6.1/4.6	14.2[b]/9.1[b]	49.5[b]	29.3	10.6[b]	Hermida et al[7]
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Baisse > PA nuit

Treatment of Hypertension With Chronotherapy: Is It Time of Drug Administration?

Annals of Pharmacotherapy
2015, Vol. 49(3) 323–334

Percentage Nondipper

Table 1. Summary of BP and Cardiovascular Outcomes in Prospective Chr

Population (n)	Follow-up (Mean)	Baseline 48-Hour BP, Mean	Awake-BP Reduction: Morning Admin	Awake-BP Reduction: Bedtime Admin	Asleep-BP Redu: Morning Admin	Asleep-BP Redu: Be A	Percentage Nondipper: Morning Admin	Percentage Nondipper: Bedtime Admin	te CVD ne[a] (%): Bedtime Admin	Reference
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[a]Composite CVD outcome: all-cause death, myocardial infarction, angina pectoris, coronary revascularization, heart failure, acute arterial occlusion of the lower extremities, rupture of aortic aneurisms, thrombotic occlusion of the retinal artery, hemorrhagic stroke, ischemic stroke, and transient ischemic attack.

[b]Statistically significant between treatment groups.

Meilleur dipping

Treatment of Hypertension With Chronotherapy: Is It Time of Drug Administration?

Annals of Pharmacotherapy
2015, Vol. 49(3) 323–334

Table 1. Summary of BP and Cardiovascular Outcomes in Prospective Chronotherapy

Population (n)	Follow-up (Mean)	Baseline 48-Hour BP, Mean	Awake-BP Reduction: Morning Admin	Awake-BP Reduction: Bedtime Admin	Asleep-BP Reduction: Morning Admin	Asleep-BP Reduction: Bedtime Admin	Composite CVD Outcome[a] (%): Morning Admin	Composite CVD Outcome[a] (%): Bedtime Admin	Reference
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[b]Statistically significant between treatment groups.

Résultats positifs mais venant d'un même centre

Réduction des complications CV

Bedtime hypertension treatment improves cardiovascular risk reduction: the Hygia Chronotherapy Trial

ESC European Society of Cardiology
European Heart Journal (2019) **0**, 1–12
doi:10.1093/eurheartj/ehz754

Suivi 6 ans

But étude multicentrique: tester l'effet sur les complications CV de l'administration des médicaments antiHTA, soit le matin soit le soir au coucher en MG

Population et méthodologie: >19000 patients 60 ans HT, la moitié recevant le traitement le matin et l'autre moitié le soir avec MAPA de 48 h chaque année,

Résultats: amélioration du contrôle de la PA/24h et de nuit avec plus de dipping si prise le soir des médicaments antiHTA et beaucoup moins de complications CV!

Bedtime hypertension treatment improves cardiovascular risk reduction: the Hygia Chronotherapy Trial

Hermida et al

European Heart Journal (2019) **0**, 1–12
doi:10.1093/eurheartj/ehz754

Table 1 **Baseline characteristics of participants categorized according to treatment-time regimen (either upon awakening or at bedtime)**

Variable	All	Awakening	Bedtime	*P* between groups
Demographic and clinical characteristics				
Participants, *n*	19 084	9552	9532	
Age, years	60.5 ± 13.7	60.5 ± 13.9	60.6 ± 13.5	0.831
Sex, % men	55.6	56.2	55.0	0.086
Height, cm	162.9 ± 9.6	163.0 ± 9.7	162.8 ± 9.5	0.059
Weight, kg	79.0 ± 15.2	78.9 ± 15.3	79.0 ± 15.1	0.518
BMI, kg/m^2	29.7 ± 4.8	29.6 ± 4.8	29.7 ± 4.7	0.030
Waist, cm	101.3 ± 12.2	101.2 ± 12.3	101.3 ± 12.2	0.850
Night-time sleep duration, h	8.8 ± 1.3	8.8 ± 1.4	8.8 ± 1.3	0.156
Type 2 diabetes, %	23.9	23.7	24.1	0.484
Obstructive sleep apnoea, %	4.1	4.2	3.9	0.374
Smoking, %	15.2	15.6	14.8	0.129
Obesity, %	43.0	42.6	43.5	0.180
Chronic kidney disease, %	29.4	29.9	28.9	0.141
Previous CVD events, %	10.4	10.8	10.0	0.054
Hypertension treatment, %	57.4	57.9	56.9	0.166

Table 1 Baseline characteristics of participants categorized according to treatment-time regimen (either upon awakening or at bedtime)

Variable	All	Awakening	Bedtime	*P* between
Office[a] and ambulatory BP				
Office SBP, mmHg	149.4 ± 20.1	149.4 ± 20.5	149.5 ± 19.9	0.987
Office DBP, mmHg	86.1 ± 12.1	86.3 ± 11.9	86.0 ± 12.3	0.276
Office PP, mmHg	63.3 ± 17.0	63.1 ± 17.0	63.5 ± 16.9	0.351
Office heart rate, beats/min	72.8 ± 12.3	73.1 ± 12.5	72.6 ± 12.2	0.064
Awake SBP mean, mmHg	136.0 ± 14.4	136.1 ± 14.9	135.9 ± 14.0	0.449
Asleep SBP mean, mmHg	123.6 ± 15.2	123.3 ± 16.0	123.7 ± 14.6	0.138
48 h SBP mean, mmHg	131.6 ± 13.8	131.4 ± 14.4	131.7 ± 13.3	0.306
Sleep-time relative SBP decline, %	9.0 ± 7.8	9.3 ± 7.9	9.0 ± 7.6	0.000
Awake DBP mean, mmHg	81.3 ± 11.3	81.3 ± 11.5	81.3 ± 11.2	0.955
Asleep DBP mean, mmHg	70.2 ± 10.1	70.1 ± 10.2	70.3 ± 10.0	0.420
48 h DBP mean, mmHg	77.4 ± 10.4	77.2 ± 10.6	77.5 ± 10.3	0.104
Sleep-time relative DBP decline, %	13.3 ± 8.4	13.3 ± 8.7	13.2 ± 8.2	0.468
Non-dipper, %	49.3	49.0	49.5	0.363

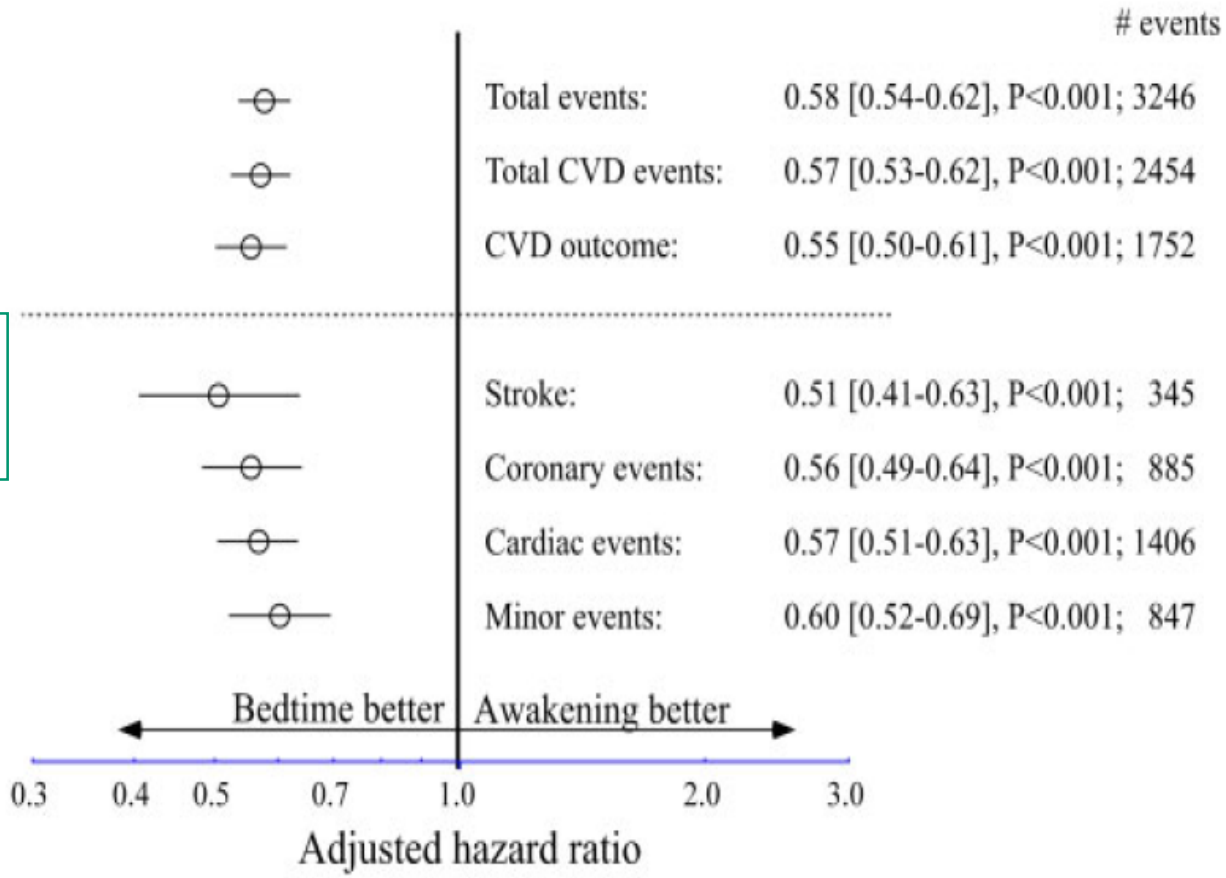
European Heart Journal (2019) **0**, 1–12
doi:10.1093/eurheartj/ehz754

Table 2 Final characteristics of participants categorized according to treatment-time regimen (either upon awakening or at bedtime)

Variable	Awakening	Bedtime	*P* between groups
Participants, *n*	9552	9532	
Hypertension treatment			
Number of medications	1.80 ± 0.89	1.71 ± 0.93	<0.001
ARB, %	53.1	53.1	0.995
ACEI, %	25.3	23.4	0.002
CCB, %	32.7	36.8	<0.001
β-Blocker, %	22.0	17.5	<0.001
Diuretic, %	46.5	39.5	<0.001
Office SBP, mmHg	143.2 ± 20.9	140.0 ± 20.6	<0.001
Office DBP, mmHg	82.4 ± 12.3	81.4 ± 12.4	<0.001
Office PP, mmHg	60.8 ± 17.9	58.6 ± 17.9	<0.001
Office heart rate, beats/min	71.9 ± 12.5	72.4 ± 12.5	0.078
Awake SBP mean, mmHg	129.5 ± 14.7	129.2 ± 13.4	0.294
Asleep SBP mean, mmHg	118.0 ± 16.6	114.7 ± 14.6	<0.001
48 h SBP mean, mmHg	125.6 ± 14.5	124.3 ± 12.9	<0.001
Sleep-time relative SBP decline, %	8.5 ± 8.4	12.2 ± 7.7	<0.001

Bedtime hypertension treatment reduces CVD risk

50% sur AVC!!



Take home figure Adjusted hazard ratio (95% CI) of cardiovascular events as a function of hypertension treatment-time

Ramón C. Hermida

European Heart Journal (2019) **0**, 1–12
doi:10.1093/eurheartj/ehz754

Optimal Time to Administer Once-Daily Oral Cardiovascular Agents: Evidence Based on Randomized Clinical Trials in the Last Ten Years

Shu-yi et al. J Geriatr Med Gerontol 2018, 4:057

Methods: Focusing on chronotherapeutic topic, a literature search on randomized controlled trials (RCTs) of oral once-daily cardiovascular agents was conducted using PubMed, Cochrane Library, Scopus and Web of Science from Jan 01, 2008 to Sept 30, 2018.

Results: Forty-seven RCTs investigated cardiovascular agents. Thirty-five RCTs showed the advantages of evening or bedtime dosing, only one RCT showed the superiority of morning dosing (perindopril for patients with obstructive sleep apnoea and hypertension), and 11 RCTs showed no relationship between dosing time and therapeutic outcomes.

Poulter et al Impact of AM or PM Dosing on 24-Hour BP Levels

Hypertension. 2018;72:870-873.

Table 1. Baseline Characteristics by Order of Dosing Schedule

Variable*	Evening/Morning	Morning/Evening	Total
Number, N	52	51	103
Age	62.8 (9.7)	61.8 (11.0)	61.8 (10.3)
Female, N (%)	21 (40)	24 (47)	45 (44)
BMI	29.1 (5.6)	29.1 (4.7)	29.1 (5.2)
Heart rate	72.8 (10.3)	72.7 (9.6)	72.7 (9.9)
Systolic BP	127.1 (8.7)	129.0 (8.8)	128.0 (8.8)
Diastolic BP	76.6 (6.1)	76.3 (6.2)	76.4 (6.1)
Current smoker, N (%)	4 (8)	8 (16)	12 (12)
Alcohol units per week	16.7 (17.2)	11.8 (11.9)	14.6 (15.2)
Fasting plasma glucose	5.6 (0.9)	5.5 (1.0)	5.6 (0.9)
Non-HDL cholesterol	3.4 (1.0)	3.5 (1.0)	3.5 (1.0)

Eligible patients were randomized to receive their usual medications in the morning (6 AM–11 AM) or in the evening (6 PM–11 PM) for 12 weeks at which point they crossed over to evening and morning dosing,

Table 2. BP Levels (mm Hg) by Timing of Dosing Schedules

Outcome	Baseline (n=95)	Drug taken		Observed difference	Adjusted* Difference (95% CI)
		Morning (n=95)	Evening (n=97)		
24h Systolic BP	128.64 (9.18)	129.65 (10.66)	129.75 (12.75)	0.10	0.11 (–3.20, 3.42)
24h Diastolic BP	76.92 (6.50)	77.24 (7.22)	77.99 (8.20)	0.75	0.77 (–1.38, 2.91)
Day time SBP	131.16 (9.98)	132.24 (10.86)	132.77 (12.87)	0.53	0.54 (–2.82, 3.89)
Day time DBP	79.14 (7.03)	79.27 (7.73)	80.55 (8.51)	1.28	1.30 (–0.96, 3.56)
Night time SBP	120.89 (10.79)	122.76 (12.18)	121.08 (14.92)	–1.68	–1.62 (–5.38, 2.15)
Night time DBP	69.83 (7.52)	70.92 (9.68)	70.57 (9.67)	–0.35	–0.32 (–2.81, 2.17)
Clinic SBP	128.07 (8.97)	129.37 (11.21)	129.81 (12.53)	0.44	0.39 (–2.91, 3.69)
Clinic DBP	76.54 (5.88)	77.26 (7.12)	77.41 (8.36)	0.15	0.14 (–2.03, 2.32)
Quality of Life Score	82.80 (11.89)	84.14 (11.45)	84.04 (10.25)	–0.10	–0.12 (–3.12, 2.89)

BP indicates blood pressure; DBP, diastolic BP; QoL, quality of life; and SBP, systolic BP.

*Site, period (visit), and sequence (group)

Randomized Crossover Trial of the Impact of Morning or Evening Dosing of Antihypertensive Agents on 24-Hour Ambulatory Blood Pressure

The HARMONY Trial

Neil R. Poulter, Christos Savopoulos, Aisha Anjum, Martha Apostolopoulou, Neil Chapman, Mary Cross, Emanuela Falaschetti, Spiros Fotiadis, Rebecca M. James, Ilias Kanellos, Matyas Szigeti, Simon Thom, Peter Sever, David Thompson, Apostolos I. Hatzitolios

Hypertension. 2018;72:870-873.

(≤65/≥65 years) or sex did not affect results. In summary, among hypertensive patients with reasonably well-controlled blood pressure, the timing of antihypertensive drug administration (morning or evening) did not affect mean 24-hour or clinic blood pressure levels.

Résultats neutres de la chronothérapie mais pas de données sur les médicaments utilisés et patients déjà normalisés sur le plan de la PA au départ!

Chronothérapie et HTA

- La PA nocturne est très prédictive du pronostic CV.
- Donc la MAPA est souhaitable dans la bonne prise en charge d'une HTA, en complément de l'automesure quand traitement stabilisé (surtout chez le diabétique, l'IRC, le sujet avec SAS).
- En pratique, pour traiter un hypertendu, utilisez des **médicaments à longue durée d'action, à pleine dose, éventuellement en association.**
- Penser, si non dipping, HTA nocturne ou PA élevée au lever, à déplacer une prise médicamenteuse antiHTA le soir ou à ajouter un traitement au coucher.

Management of morning hypertension: a consensus statement of an Asian expert panel

J Clin Hypertens. 2018;20:39–44.

TABLE 2 Commonly used oral antihypertensive drugs

Class and drug	Biological half-life, h	Daily dose, mg	No. of doses per
Angiotensin-converting enzyme inhibitor			
Benazepril	11	10–40	1 or 2
Captopril	1.9	50–150	2
Enalapril	11	2.5–40	1 or 2
Lisinopril	12	10–40	1
Perindopril	17	2–8	1
Ramipril	4	2.5–20	1 or 2
Angiotensin receptor blocker			
Candesartan	9	4–32	1
Irbesartan	15	75–300	1
Losartan	2	25–100	1 or 2
Olmesartan	13	10–40	1
Telmisartan	24	20–80	1
Valsartan	6	80–320	1
β-Blocker			
Atenolol	7	25–100	1
Bisoprolol	12	2.5–10	1
Metoprolol	3–7	50–200	1 or 2
Dihydropyridine calcium channel blocker			
Amlodipine	30–55	2.5–10	1
Felodipine ER	11–17	1.5–10	1
Lacidipine	13–19	2–4	1
Lercanidipine	8–10	10–20	1
Nifedipine GITS	2	20–80	1
Nitrendipine	8–24	10–40	1 or 2
Thiazide diuretic			
Chlorthalidone	40	25–50	1
Hydrochlorothiazide	5.6–14.8	12.5–50	1 or 2
Indapamide	14–18	1.25–5	1

Ou prescrire une bithérapie pour les autres molécules

Evening versus morning dosing of antihypertensive drugs in hypertensive patients with sleep apnoea: a cross-over study

Alexandros Kasiakogias[a], Costas Tsioufis[a], Costas Thomopoulos[a], Ioannis Andrikou[a], Dimitrios Aragiannis[a], Kyriakos Dimitriadis[a], Dimitrios Tsiachris[a], Grzegorz Bilo[b], Skevos Sideris[a], Konstantinos Filis[c], Gianfranco Parati[b], and Christodoulos Stefanadis[a]

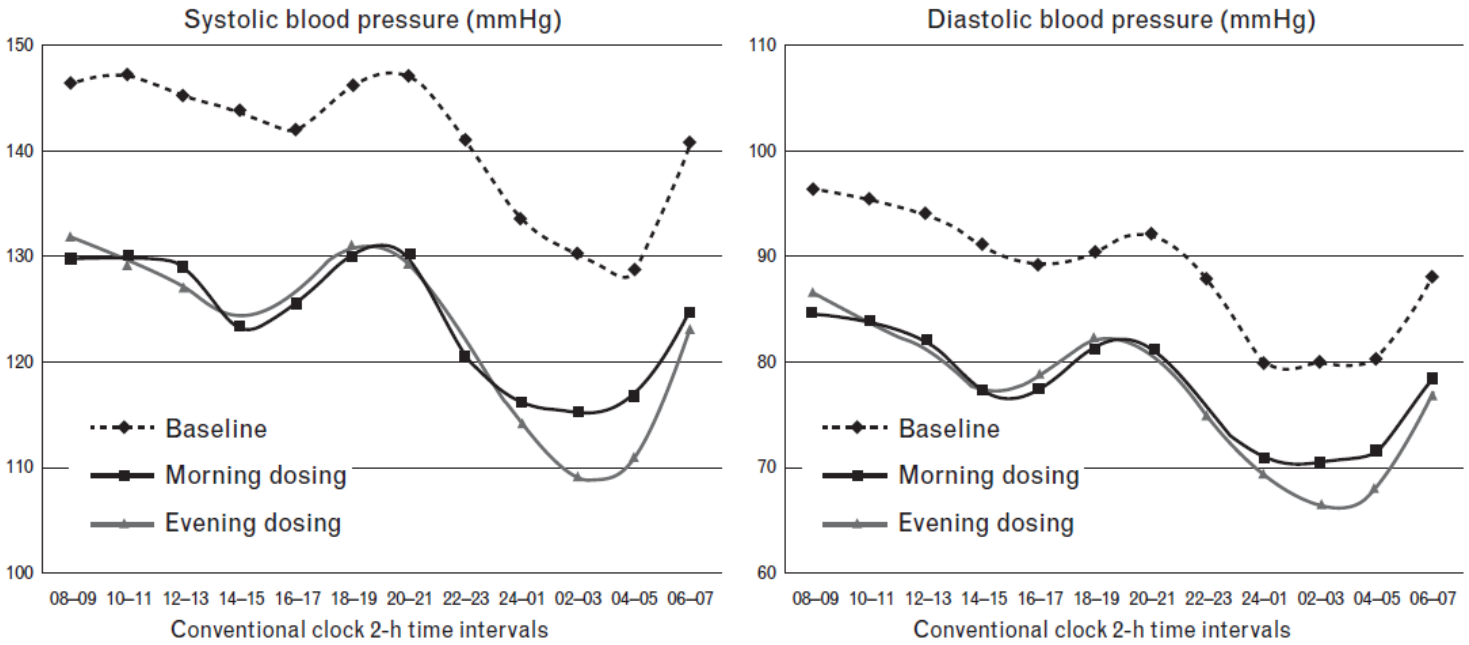


FIGURE 3 Ambulatory SBP and DBP curves at baseline (dotted line), after morning dosing (black line) and after evening dosing (grey line) of antihypertensive treatment prescribed in our study, presented as two-hourly means.

Conclusion: Evening dosing of antihypertensive drugs improves night-time BP and dipping status in nonsleepy patients with OSA, irrespective of CPAP application.

Journal of Hypertension 2015, 33:393–400

Chronothérapie dans le traitement de l'hypertension artérielle:
Utile? Oui dans certains cas, mais à individualiser selon MAPA