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www.swisshypertension.ch

HYPERTENSION ARTERIELLE
Prise en charge en 2020: nouveautés?

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Mme C – 65 ans

Patiente avec IRC stade 3bA1 (eGFR 40ml/min et albU<30mg/g)

- Diabète type 2 NIR – Hb A1c 8.0%
- HTA traitée depuis 10 ans

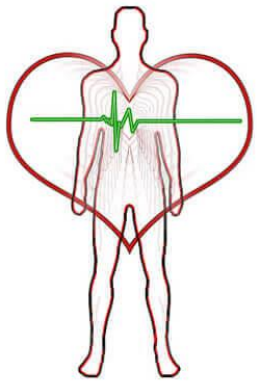
TA fluctuantes à domicile: 120/80 → 200/100mmHg

TTT: lisinopril 20mg, carvedilol 12.5mg 2x/j
metformine 1g 2x/j

Status: TA G 127/74mmHg. TA D 130/80mmHg.
poids 70kg pour 1m60 (BMI 27.3kg/m^2)

Plan

- ✓ Epidémiologie
- ✓ Nouvelles définitions/recommandations
- ✓ Mesure ambulatoire pression artérielle
- ✓ Indication à Traitement – cibles
- ✓ Nouveautés thérapeutiques ?

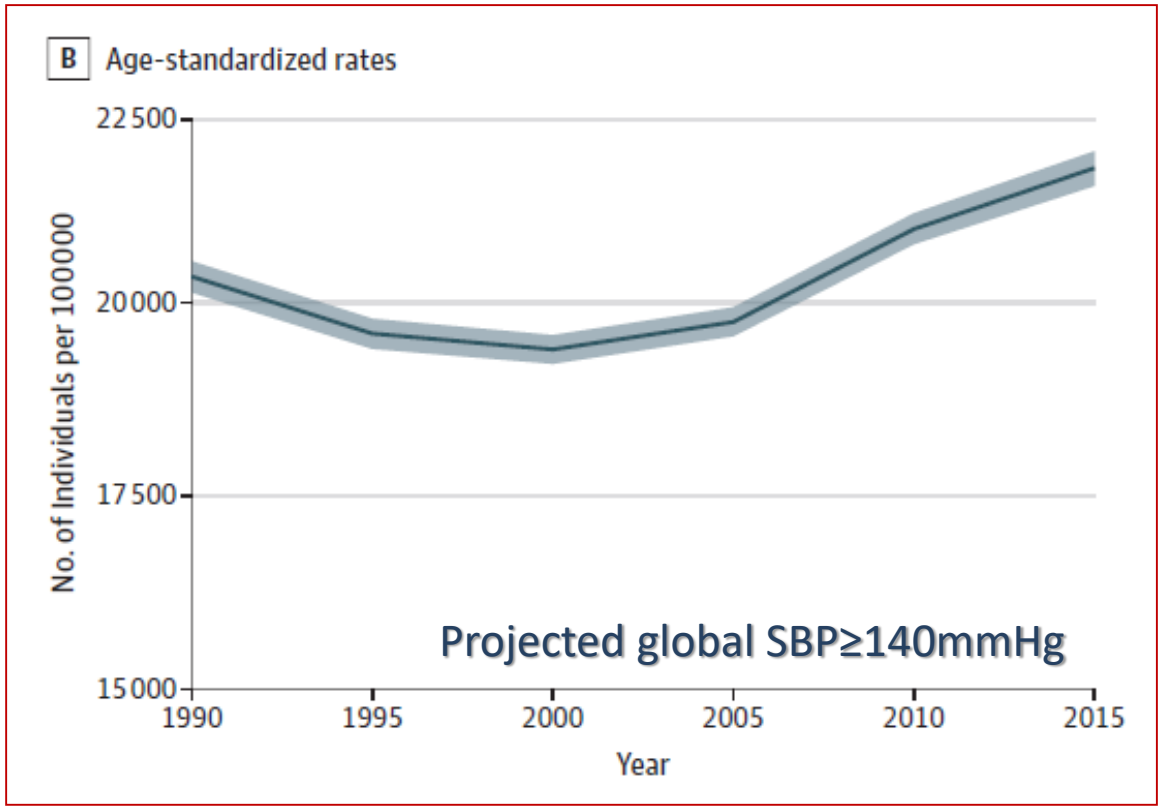


Contexte épidémiologique

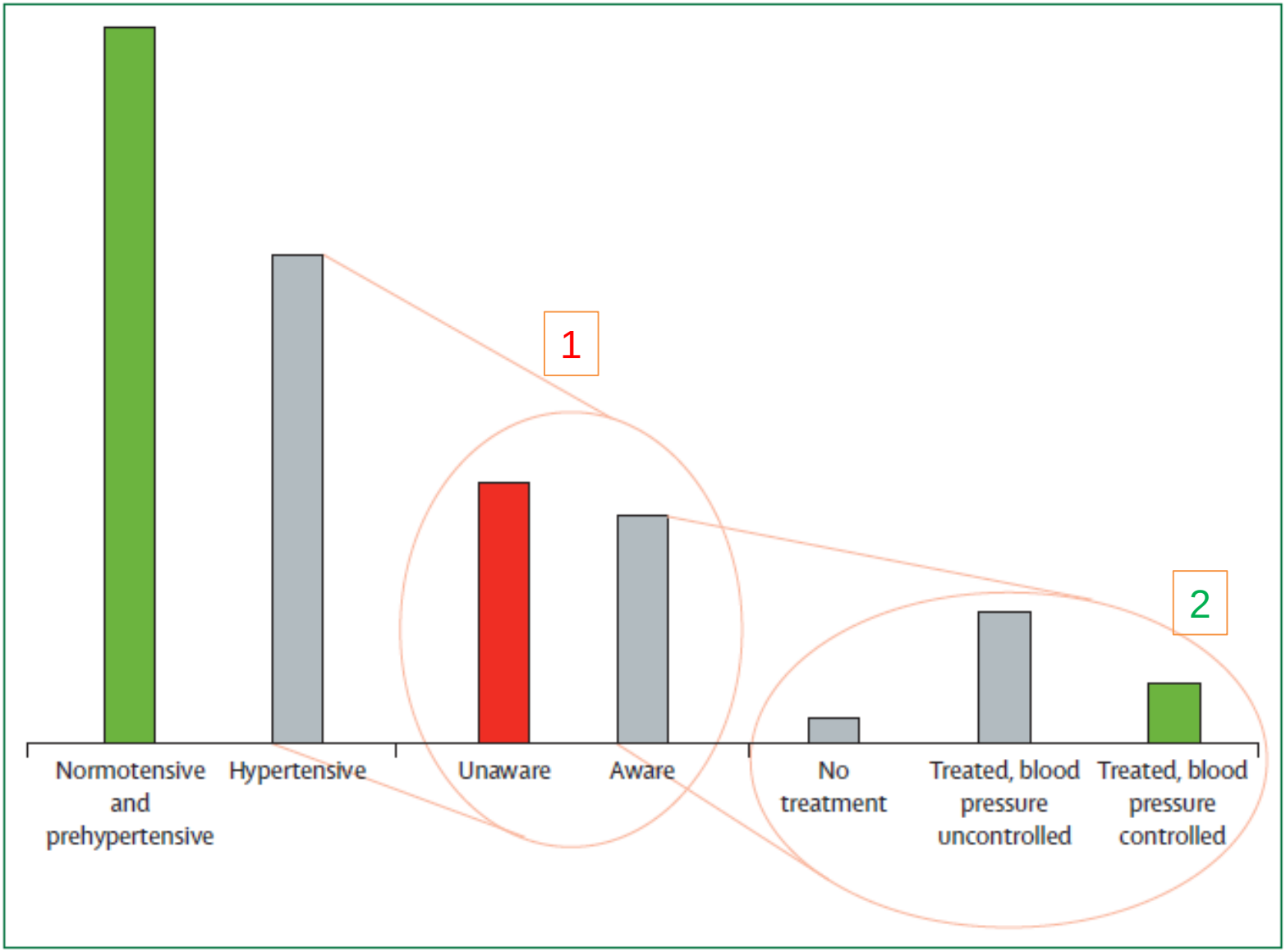
Projections 2015-2025: 1.6 milliards d'hypertendus

- HTA =principal facteur de mortalité précoce et morbidité

  →10'326'000 décès/an en lien direct avec HTA



JAMA. 2017;317(2):165-182.
Lancet. 2016;388(10053): 1659.
JAMA. 2013;310(9):959-968



1. 53.5% avec HTA → pas conscient de HTA

2. 13% HTA traités →TA contrôlée (<140mmHg)

Lancet 2016; 388: 2665–712

Effet du traitement sur maladie CV et mortalité

Meta-analyse 123 études (n=613'815):

↓PA syst 10mmHg réduit risque relatif

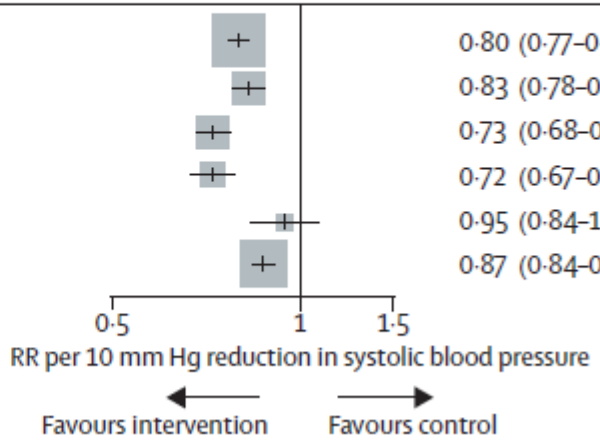
→ événements CV (-20%)

→ maladie coronarienne (-17%)

→ AVC (-27%)

→ Insuffisance cardiaque (-28%)

	Studies	Intervention		Control		RR (95% CI) per 10 mm Hg reduction in systolic blood pressure
		Events	Participants	Events	Participants	
Major cardiovascular events	55	13209	137319	14068	128259	0·80 (0·77–0·83)
Coronary heart disease	56	4862	136986	5301	128548	0·83 (0·78–0·88)
Stroke	54	4635	136682	5378	128641	0·73 (0·68–0·77)
Heart failure	43	3284	115411	3760	107440	0·72 (0·67–0·78)
Renal failure	16	890	39888	834	39043	0·95 (0·84–1·07)
All-cause mortality	57	9775	138298	9998	129700	0·87 (0·84–0·91)

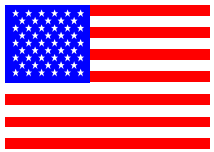


Lancet 2016; 387- 957-967

Définitions et seuils de l'hypertension

Définitions basée sur TA en clinique: pas de modifications

Catégorie	Systolique mmHg		Diastolique mmHg
Optimale	< 120	et	< 80
Normale	120-129	et/ou	80-84
Normale haute	130-139	et/ou	85-89
HTA stade 1	140-159	et/ou	90-99
HTA stade 2	160-179	et/ou	100-109
HTA stade 3	≥ 180	et/ou	≥ 110
HTA systolique isolée	≥ 140	et	< 90



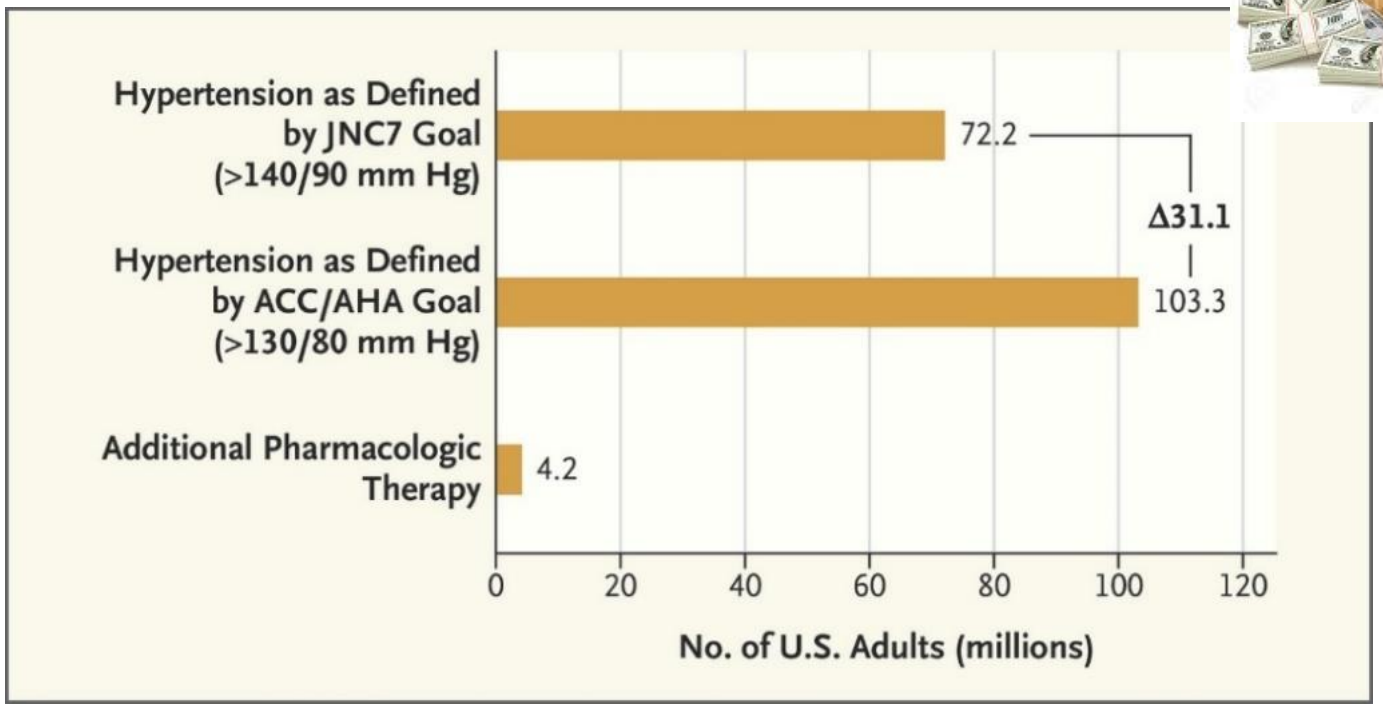
Dans recommandations US: TA≥130/80mmHg définit stade 1
TA≥140/90mmHg définit stade 2

Jhypertension 2018: 36:

Impact définitions américaines

Prévalence HTA selon ≥140/90mmHg = 32% → 48 % si TA ≥130/80mmHg

- 39% non contrôlés → 53 % selon nouveau guidelines
- 31 millions d'US auront besoin de soins médicaux
- 4.2 millions auront besoin d'un traitement
- 29 millions devront intensifier leur traitement



Bakris, New Engl J Med January 17, 2018. Circulation. 2018;137:109

GUIDELINES 2018: modifications

2013	2018
Diagnosis	**Diagnosis**
Office BP is recommended for screening and diagnosis of hypertension.	It is recommended to base the diagnosis of hypertension on: • Repeated office BP measurements; or • Out-of-office BP measurement with ABPM and/or HBPM if logistically and economically feasible.
Treatment thresholds **High normal BP (130 –139/85–89 mmHg):** Unless the necessary evidence is obtained, it is not recommended to initiate antihypertensive drug therapy at high–normal BP.	**Treatment thresholds** **High normal BP (130 –139/85–89 mmHg):** Drug treatment may be considered when cardiovascular risk is very high due to established CVD, especially CAD.
Treatment thresholds **Treatment of low-risk grade 1 hypertension:** Initiation of antihypertensive drug treatment should also be considered in grade 1 hypertensive patients at low–moderate-risk, when BP is within this range at several repeated visits or elevated by ambulatory BP criteria, and remains within this range despite a reasonable period of time with lifestyle measures.	**Treatment thresholds** **Treatment of low-risk grade 1 hypertension:** In patients with grade 1 hypertension at low–moderate-risk and without evidence of HMOD, BP-lowering drug treatment is recommended if the patient remains hypertensive after a period of lifestyle intervention.
Treatment thresholds **Older patients** Antihypertensive drug treatment may be considered in the elderly (at least when younger than 80 years) when SBP is in the 140–159 mmHg range, provided that antihypertensive treatment is well tolerated.	**Treatment thresholds** **Older patients** BP-lowering drug treatment and lifestyle intervention is recommended in fit older patients (> 65 years but not > 80 years) when SBP is in the grade 1 range (140–159 mmHg), provided that treatment is well tolerated.

Jhypertension 2018: 36:

GUIDELINES 2018: modifications

BP treatment targets	BP treatment targets
An SBP goal of <140 mmHg is recommended.	• It is recommended that the first objective of treatment should be to lower BP to <140/90 mmHg in all patients and, provided that the treatment is well tolerated, treated BP values should be targeted to 130/80 mmHg or lower in most patients. • In patients < 65 years it is recommended that SBP should be lowered to a BP range of 120–129 mmHg in most patients.

BP treatment targets in older patients (65–80 years)	BP treatment targets in older patients (65 –80 years)
An SBP target of between 140–150 mmHg is recommended for older patients (65–80 years).	In older patients (≥ 65 years), it is recommended that SBP should be targeted to a BP range of 130–139 mmHg.
BP treatment targets in patients aged over 80 years	**BP treatment targets in patients aged over 80 years**
An SBP target between 140–150 mmHg should be considered in people older than 80 years, with an initial SBP ≥ 160 mmHg, provided that they are in good physical and mental condition.	An SBP target range of 130–139 mmHg is recommended for people older than 80 years, if tolerated.
DBP targets	**DBP targets**
A DBP target of < 90 mmHg is always recommended, except in patients with diabetes, in whom values < 85 mmHg are recommended.	A DBP target of < 80 mmHg should be considered for all hypertensive patients, independent of the level of risk and comorbidities.

Recommendation Grading							
	Grade I		Grade IIa		Grade IIb		Grade III

Mme C – 65 ans

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Diagnostic: Comment mesurer la PA?

Changes in recommendations	
2013	**2018**
Diagnosis Office BP is recommended for screening and diagnosis of hypertension.	**Diagnosis** It is recommended to base the diagnosis of hypertension on: • Repeated office BP measurements; or • Out-of-office BP measurement with ABPM and/or HBPM if logistically and economically feasible.

Mesure ambulatoire PA: Indications

Conditions in which white-coat hypertension is more common, e.g.

- Grade I hypertension on office BP measurement
- Marked office BP elevation without HMOD

Conditions in which masked hypertension is more common, e.g.

- High-normal office BP
- Normal office BP in individuals with HMOD or at high total CV risk

Postural and post-prandial hypotension in untreated and treated patients

Evaluation of resistant hypertension

Evaluation of BP control, especially in treated higher-risk patients

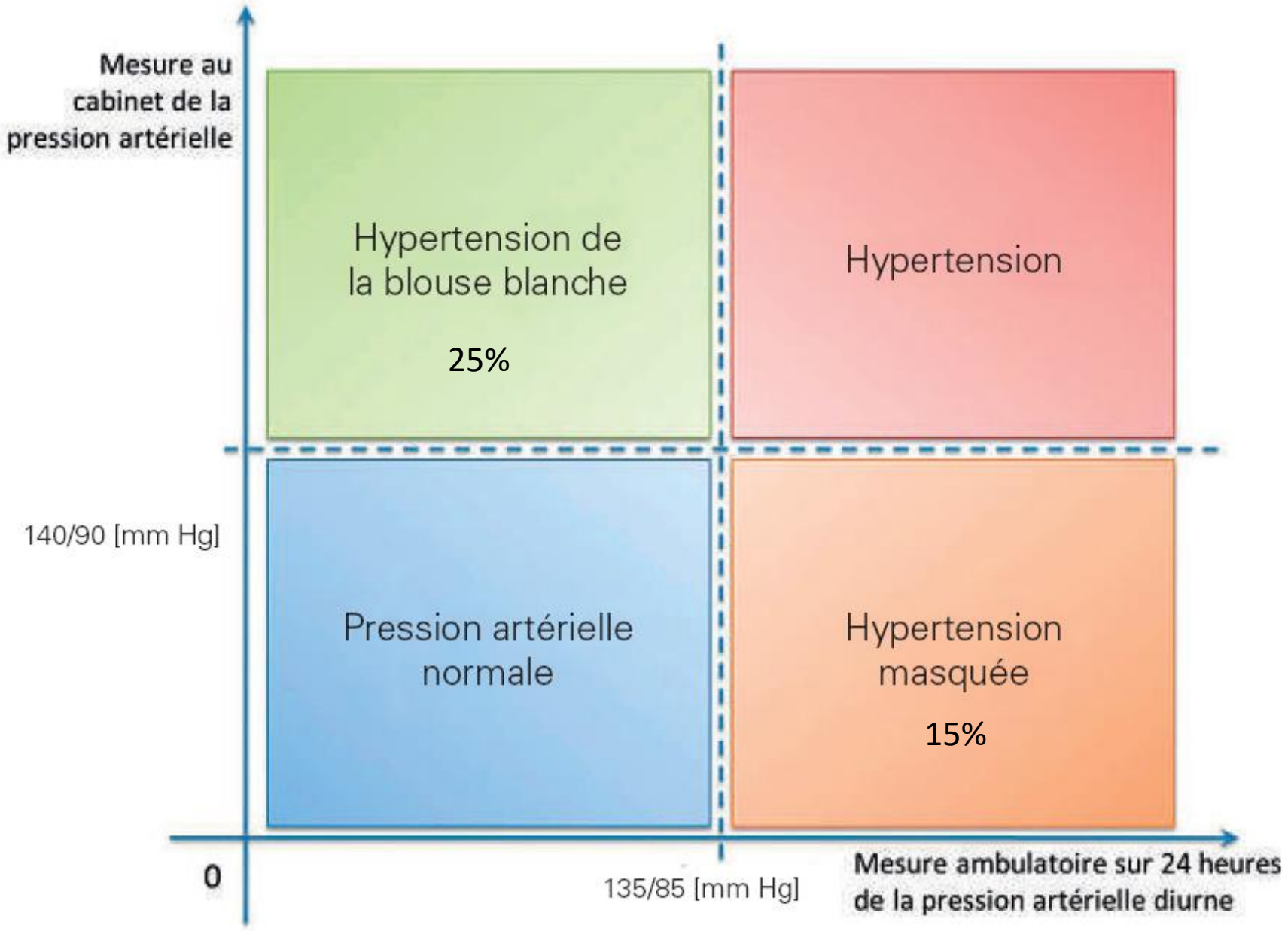
Exaggerated BP response to exercise

When there is considerable variability in the office BP

Evaluating symptoms consistent with hypotension during treatment

Specific indications for ABPM rather than HBPM:

- Assessment of nocturnal BP values and dipping status (e.g. suspicion of nocturnal hypertension, such as in sleep apnoea, CKD, diabetes, endocrine hypertension, or autonomic dysfunction)



N Gobin. Forum Médical Suisse 2012

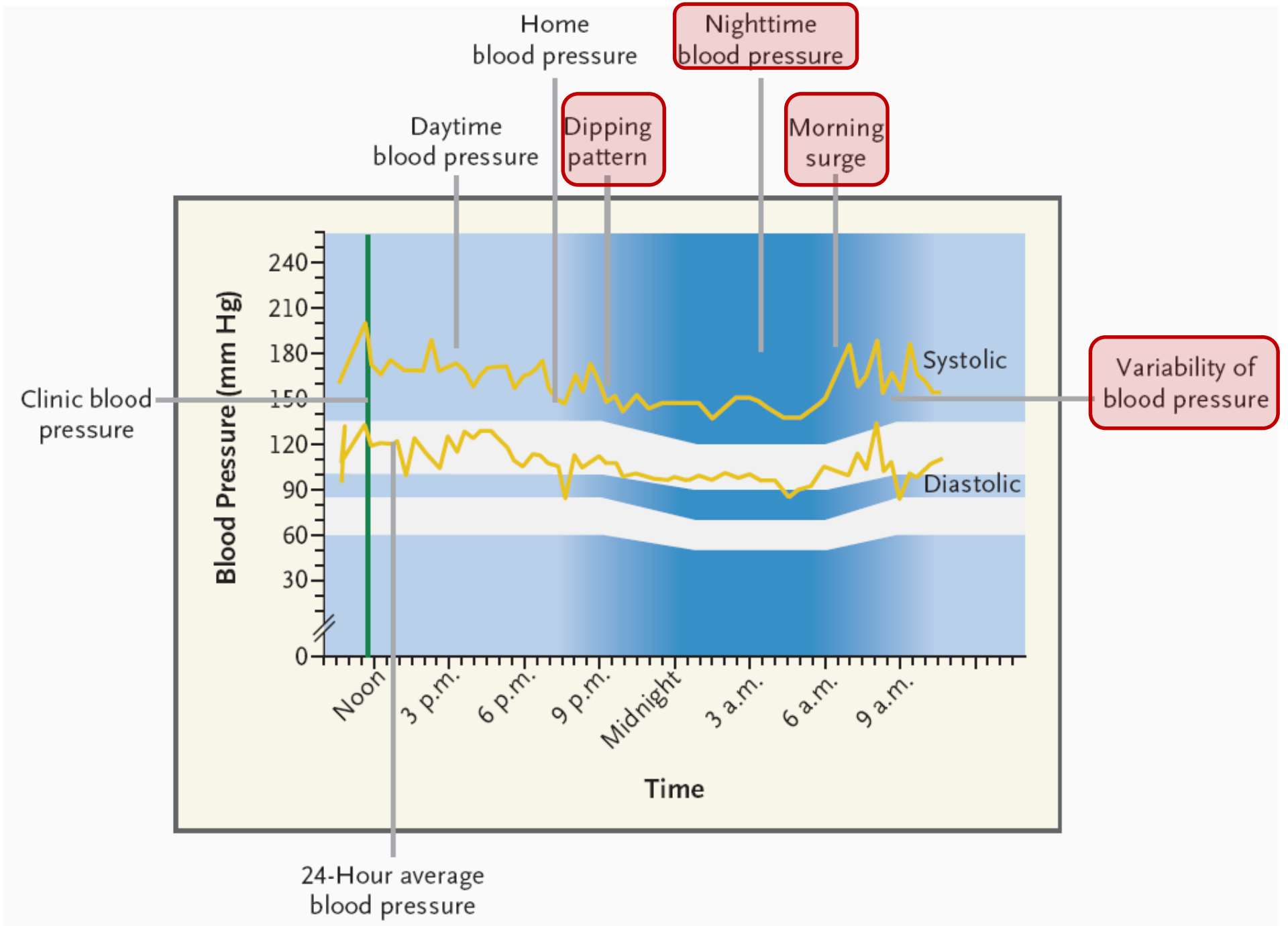
« Normes tensionnelles» selon mesure

Category	SBP (mmHg)		DBP (mmHg)
Office BP*	≥140	and/or	≥90
Ambulatory BP			
Daytime (or awake) mean	≥135	and/or	≥85
Night-time (or asleep) mean	≥120 *	and/or	≥70
24 h mean	≥130	and/or	≥80
Home BP mean	≥135	and/or	≥85

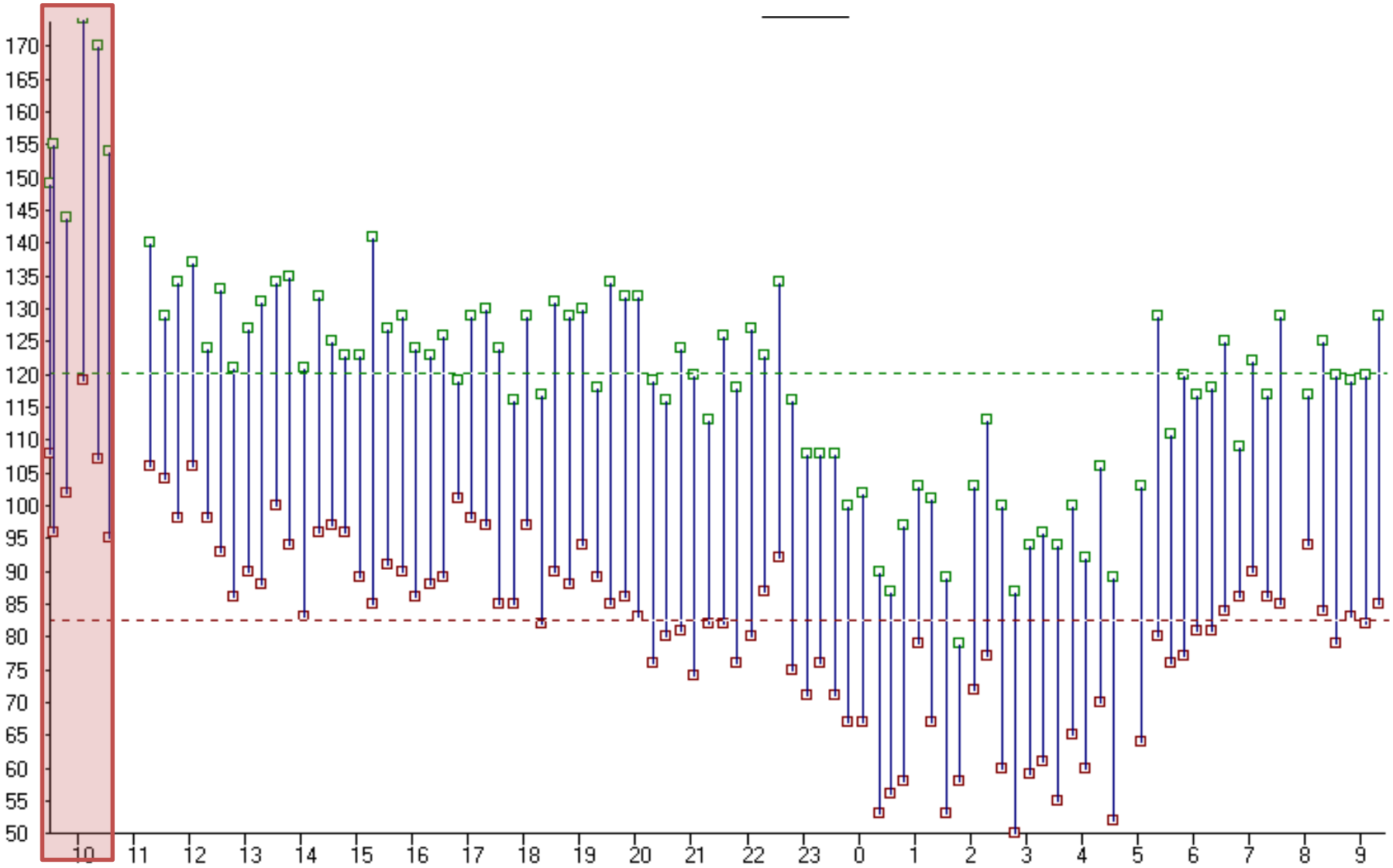
* Dipping conservé si chute PA nocturne 10-20%

Comparaison MAPA et automesure

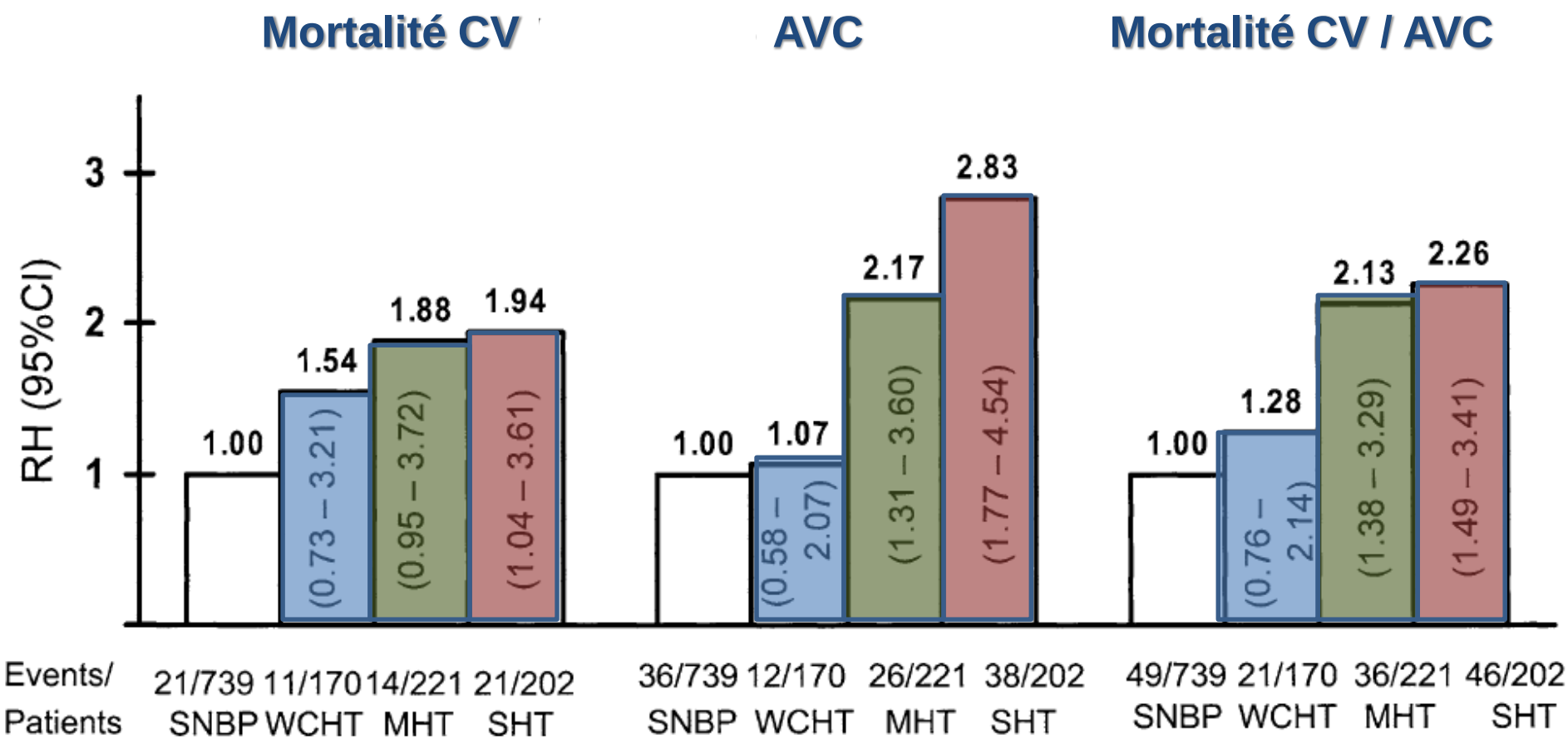
Paramètre	MAPA	Automesure
Valeur pronostique cardiaque, rénale, cérébrale	++++	+++
Détection blouse blanche	+++	++
HTA masquée	+++	++(+)
Rythme circadien, tension nocturne	++++	-
Pic matinal	++++	++
Variabilité	++++	+(+++)
Monitoring du traitement	+	++++
Coût	+++	+
Implication du patient	+	+++
Education du patient	+	+++


Home blood pressure
Nighttime blood pressure
Daytime blood pressure
Dipping pattern
Morning surge
Clinic blood pressure
Variability of blood pressure
Systolic
Diastolic
Blood Pressure (mm Hg)
240
210
180
150
120
90
60
30
0
Noon
3 p.m.
6 p.m.
9 p.m.
Midnight
3 a.m.
6 a.m.
9 a.m.
Time
24-Hour average blood pressure

Ex: HTA blouse blanche



MAPA : valeur pronostique



SNBP: PA normale soutenue

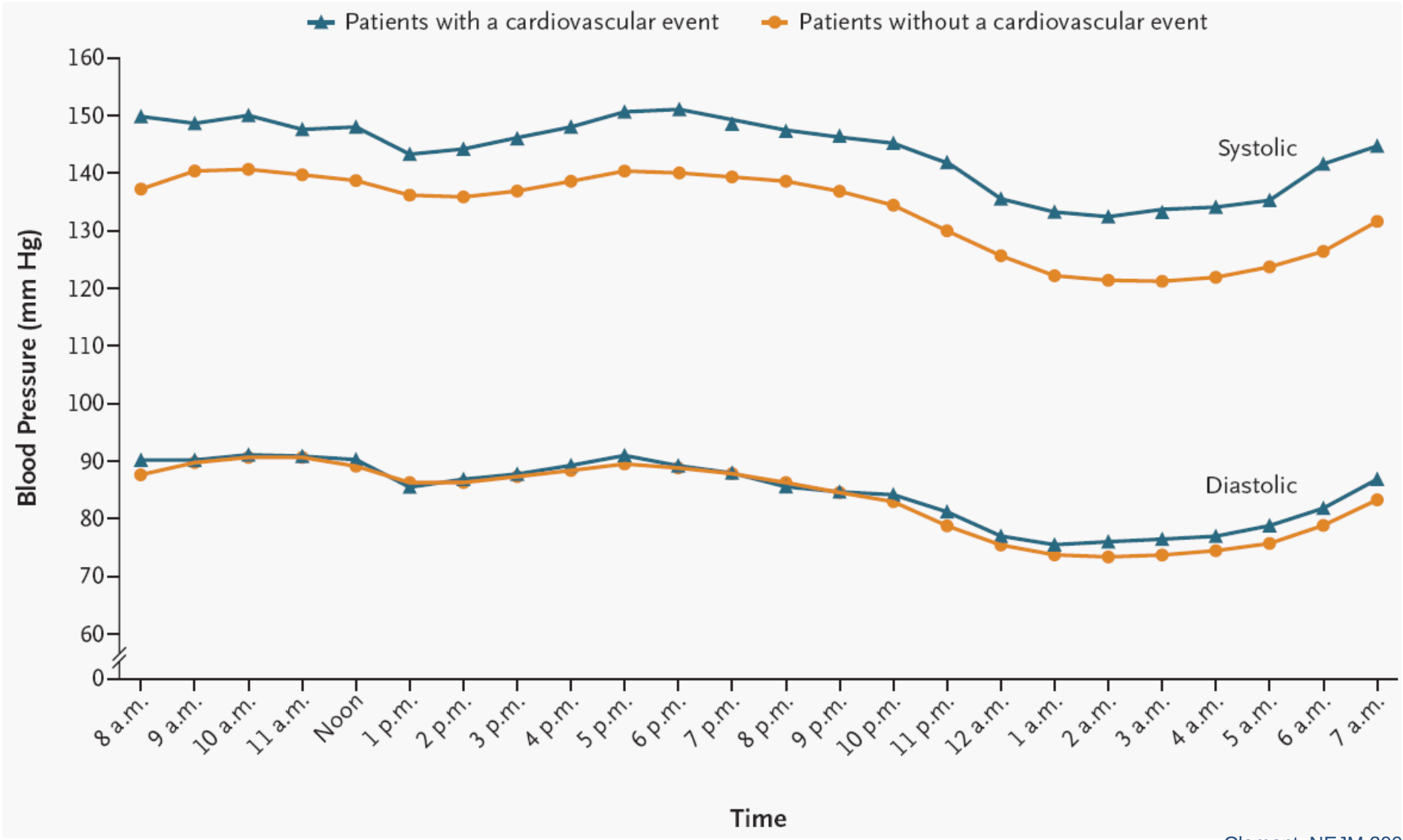
WCHT: HTA blouse blanche

MHT: HTA masquée

SHT: HTA soutenue

Ohkubo. JACC2005

MAPA prédit le risque CV



Clement. NEJM 2003

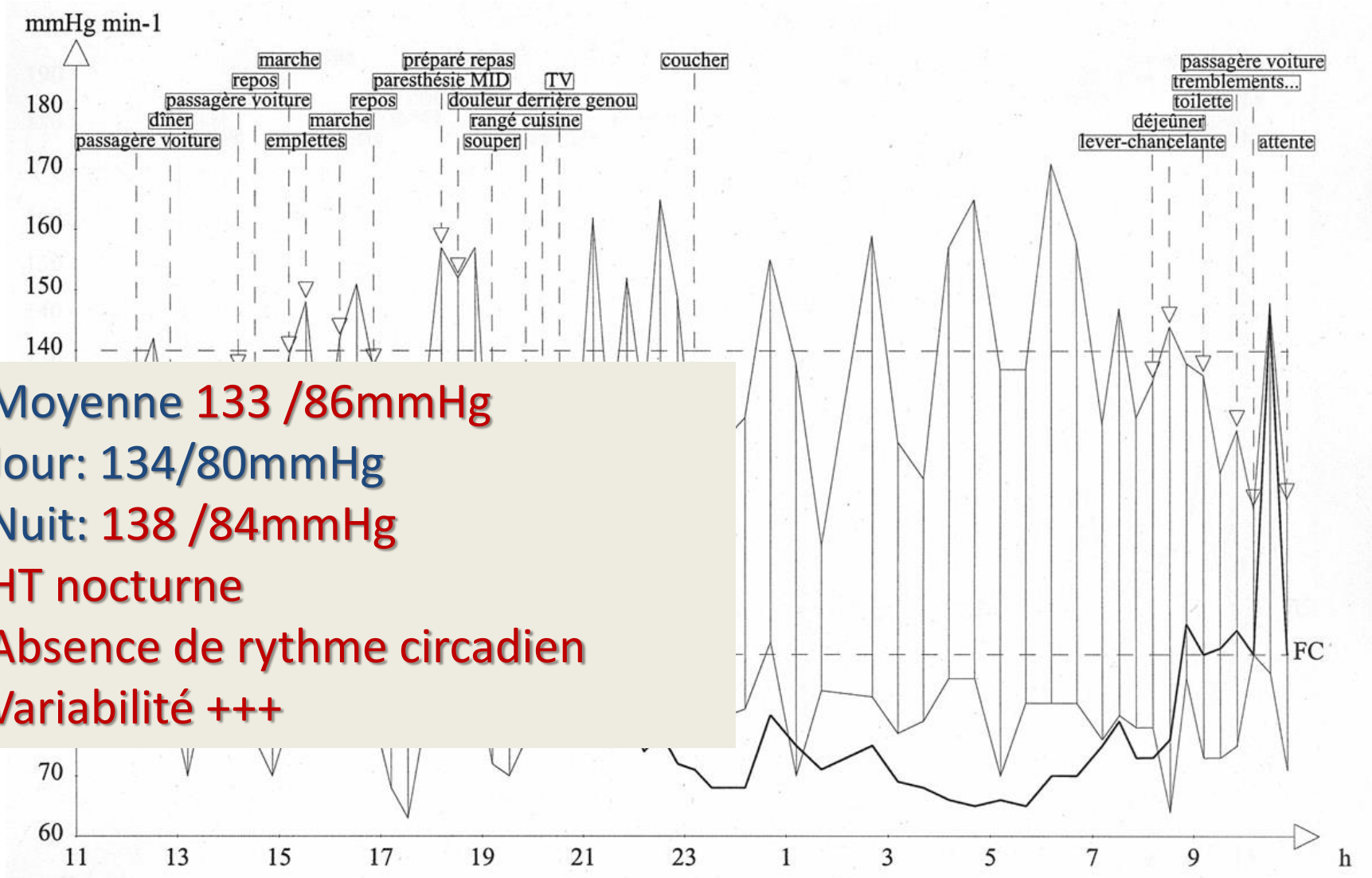
MAPA : valeur pronostique

Meilleure corrélation avec atteinte organes cibles que pression au cabinet:

- ✓ Masse ventriculaire gauche/épaisseur
- ✓ Fonction systolique et diastolique VG
- ✓ Protéinurie
- ✓ Créatinine sérique
- ✓ Plaques athéromateuse/épaisseur paroi
- ✓ Rétrécissement des artères rétininennes
- ✓ Compliance artérielle anormale
- ✓ Evénements cardio-vasculaires

Clement. NEJM 2003

Mme C – 65 ans: TA contrôlée ou pas?



Moyenne 133 /86mmHg

Jour: 134/80mmHg

Nuit: 138 /84mmHg

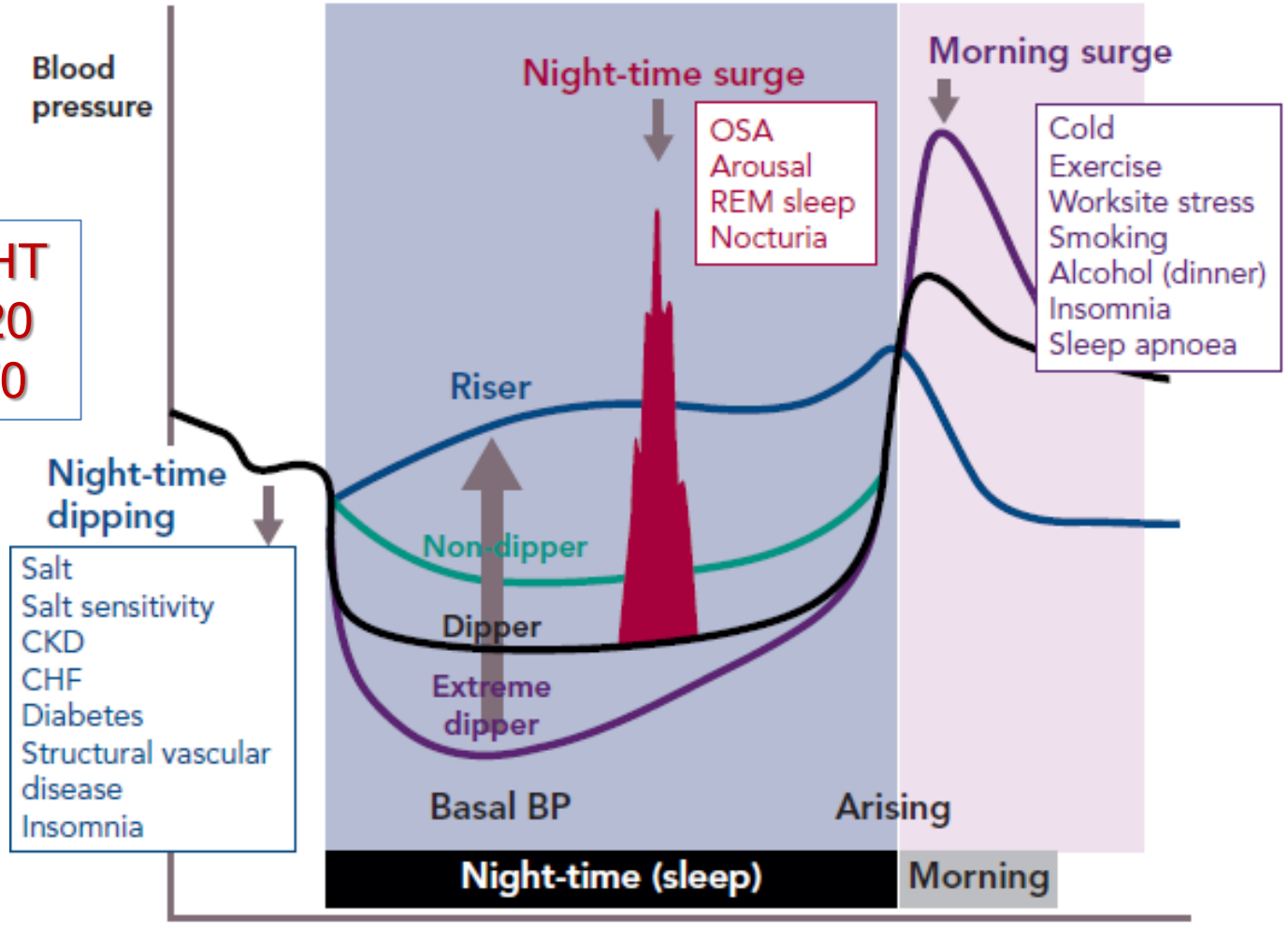
HT nocturne

Absence de rythme circadien

Variabilité +++

MAPA : diagnostic de l'HTA nocturne

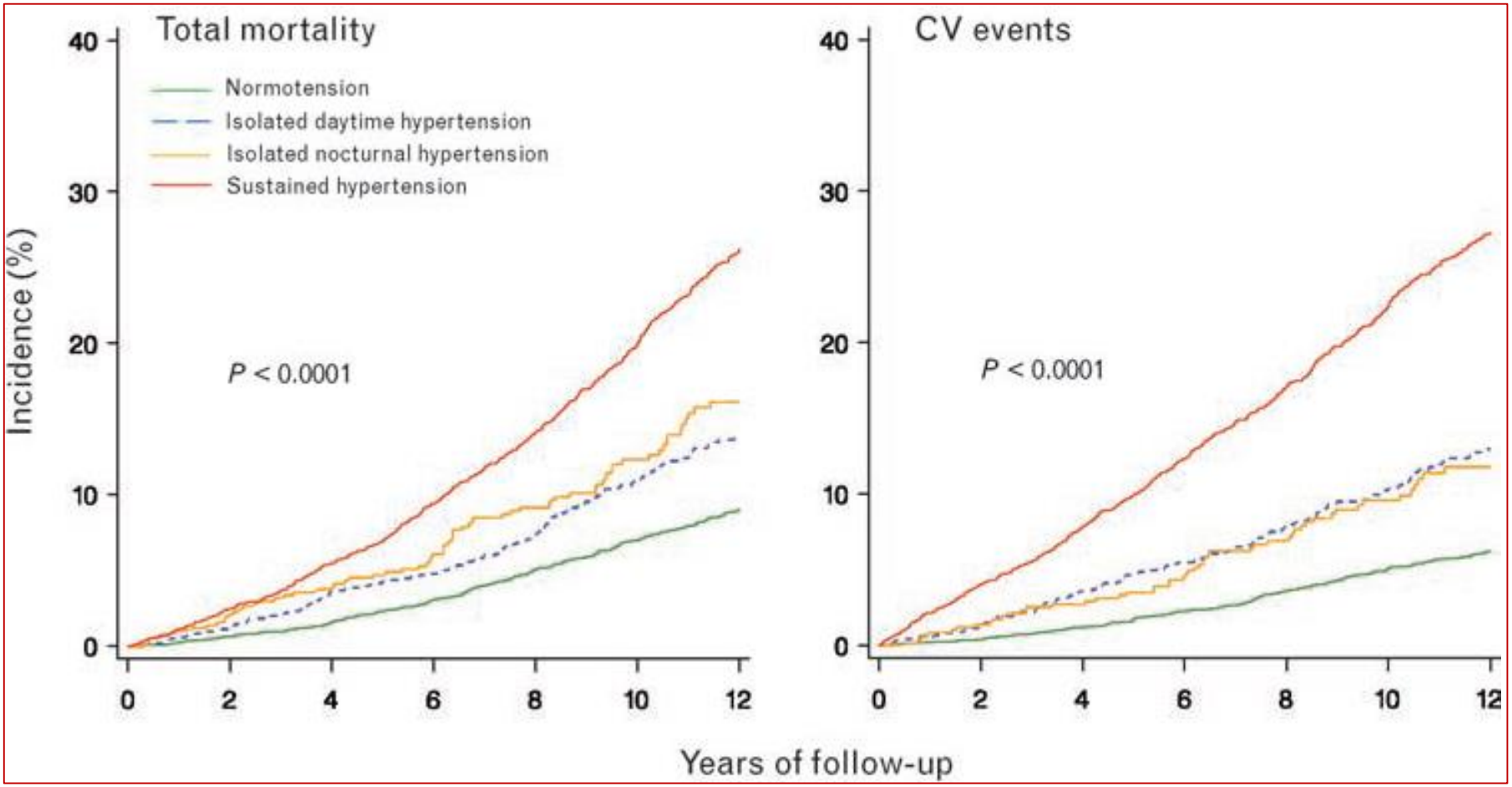
Nocturnal HT
SBP≥120
± DBP ≥70



CHF = chronic heart failure; CKD = chronic kidney disease; OSA = obstructive sleep apnoea; REM = rapid eye movement. Source: Kario et al. 2018.[8] Reproduced with permission from Wolters Kluwer Health.

Cappucio F. ECRJ 2020

Pronostic de l'HTA nocturne



Méchanismes? remodelage cardiaque, HVG, augmentation IMT, insulinoresistance

Tadic. M J Hypert 2018
Fan HQ. J Hypert 2010c

Epidémiologie – traitement HTA nocturne

Prévalence 10-20% selon population

Charactéristiques: diabète, IRC, âge – lien avec sensibilité au sel?

SAOS favorise non-dipping mais relation HTA nocturne?

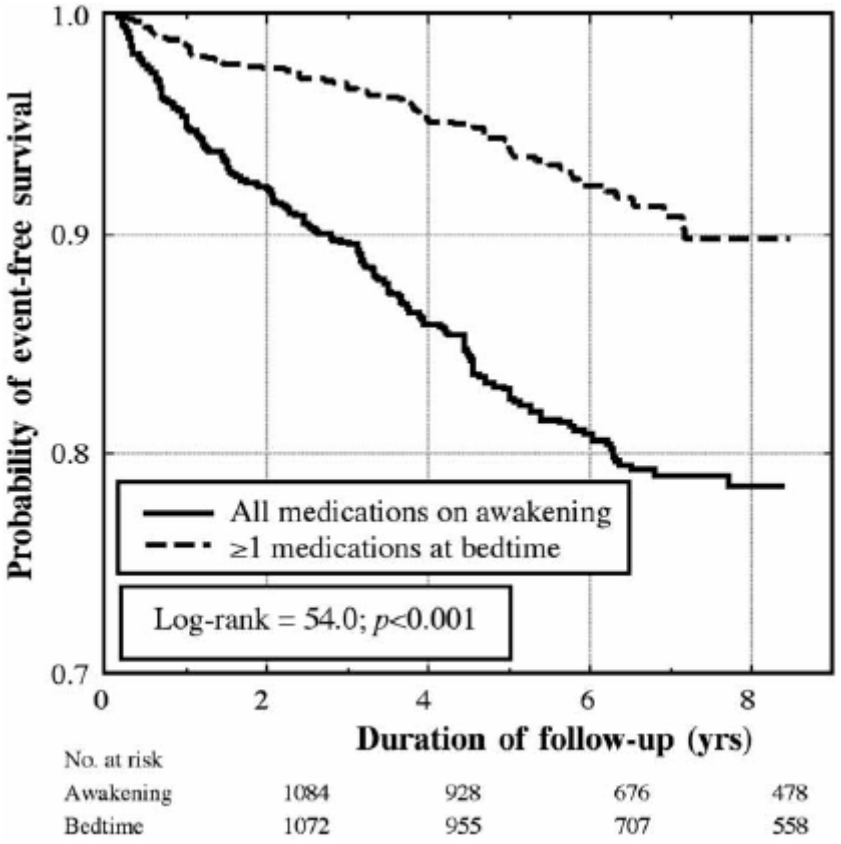
Facteurs favorisants: augmentation volume circulant
++ système sympathique
++ SRAA

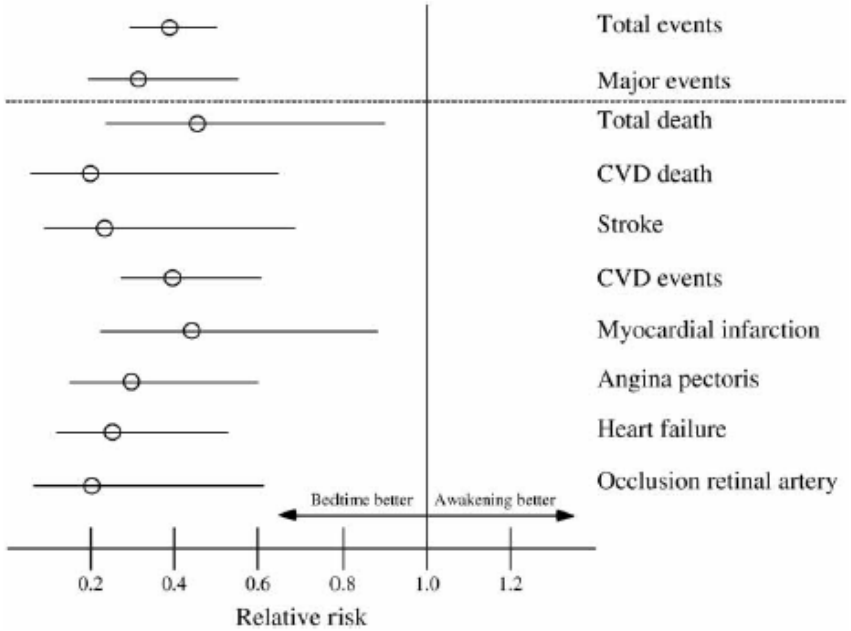
Traitements ? Restriction sodée, diurétique ?
ACEi/ARAII (+-) CCB
Chronothérapie ?
Dénervation rénale?

Uzu T, Circulation 1997
Uzu T. Circulation 1999
Fan HQ. J Hypert 2010
Kario K. NOCTURNE. Circ J 2017
Tadiq. Int BPcontrol2020

Chronothérapie

Principe: Prendre ≥ 1 medicament au coucher





34% vs 62% non dipping
Meilleur contrôle TA (62 vs 53%)

Hermida. Chronobiol 2010

Chronothérapie

ESC European Society of Cardiology

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

CLINICAL RESEARCH
Hypertension

The Hygia trial: Discussions about surprising results

On October 22, 2019 the *European Heart Journal* published a large randomized trial by Spanish investigators led by Ramon C. Hermida entitled "Bedtime hypertension treatment improves cardiovascular risk reduction: the Hygia Chronotherapy Trial" (*European Heart Journal* (2019)0, 1–12; doi:10.1093/ eurheartj/ehz754).

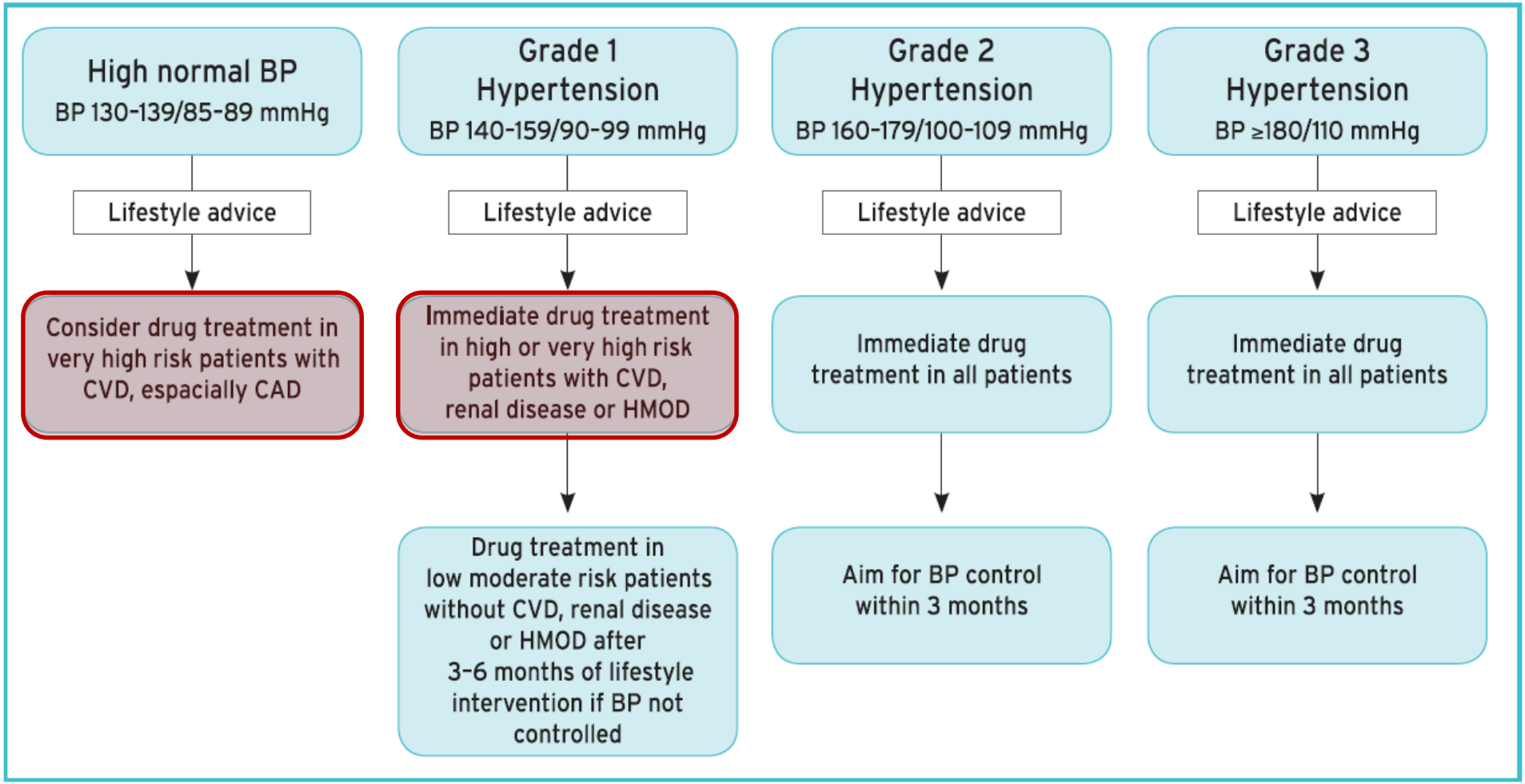
The question on when and how to apply antihypertensive drugs to patients with high blood pressure is a highly interesting scientific and clinically relevant question and has been a matter of debate for many years. In this trial the investigators randomized patients either to morning application of their antihypertensive drugs or administered antihyperten-sives in the evening.

For their study, they enrolled an impressive number of over 19 000 patients with arterial hypertension and reported an astonishing 45% reduction in the primary outcome of cardiovascular death, myocardial infarction, coronary revasculari-zation, heart failure, or stroke in those receiving their antihypertensive drugs at bedtime. Such a result is of great interest and accordingly received an enormous media echo in numerous newspapers, as well as features in television and radio shows. The topic was also discussed vividly via social media channels.

Soon after its publication online, the editors of the *European Heart Journal* received a number of critical letters, raising doubts about the conduct of the trial as well as the large effect size. Trials are often discussed, and these discussions are welcome.

In this particular case, the editors have decided to publish the majority of *Discussion Forum* contributions received thus far in order to make the raised concerns and doubts publicly available. In response to these concerns, the *ESC Journals Family Ethics Committee* has also been involved. The editors have exchanged various letters with the primary investigator in an effort to clarify outstanding issues, many of which are presented in the Discussion Forum contributions in this issue.

Indication à traitement



Atteinte d'organe: recommandations

Permet de stratifier risque HTA

- ✓ Reclassification SCORE risk

Pas forcément utile si:

- ✓ Maladie CV
- ✓ Insuffisance rénale chronique
- ✓ HTA stade 3
- ✓ Élévation cholestérol importante

Et que ces patients sont déjà sous ttt préventif (statines, aspirine, ttt HTA…)

Recommendations	Class[a]	Level[b]
Heart		
12-lead ECG is recommended for all hypertensive patients [120].	I	B
Echocardiography: • Is recommended in hypertensive patients when there are ECG abnormalities or signs or symptoms of LV dysfunction [42,134]. • May be considered when the detection of LVH may influence treatment decisions [42,134].	I IIb	B B
Blood vessels		
Ultrasound examination of the carotid arteries: • Is recommended in patients with stroke or TIA [134] • May be considered for the detection of asymptomatic atherosclerotic plaques or carotid stenosis in patients with documented vascular disease elsewhere [42].	I IIb	B B
Measurement of PWV may be considered for measuring arterial stiffness [109,189].	IIb	B
Measurement of ABI may be considered for the detection of advanced LEAD [153,190].	IIb	B
Kidney		
Measurement of serum creatinine and eGFR is recommended in all hypertensive patients [180].	I	B
Measurement of urine albumin:creatinine ratio is recommended in all hypertensive patients [43,180].	I	B
Renal ultrasound and Doppler examination should be considered in patients with impaired renal function, albuminuria, or for suspected secondary hypertension.	IIa	C
Fundoscopy		
Is recommended in patients with grades 2 or 3 hypertension and all hypertensive patients with diabetes.	I	C
May be considered in other hypertensive patients.	IIb	C
Brain		
In hypertensive patients with neurological symptoms and/or cognitive decline, brain MRI or CT should be considered for detecting brain infarctions, microbleeds, and white matter lesions [168,169].	IIa	B

Stratifications risque CV à 10 ans (SCORE)

Very high risk	**People with any of the following:**
	Documented CVD, either clinical or unequivocal on imaging . • **Clinical CVD** includes acute myocardial infarction, acute coronary syndrome, coronary or other arterial revascularization, stroke, TIA, aortic aneurysm, and PAD • **Unequivocal documented CVD on imaging** includes significant plaque (i.e. ≥ 50% stenosis) on angiography or ultrasound; it does not include increase in carotid intima-media thickness • **Diabetes mellitus with target organ damage**, e.g. proteinuria or a with a major risk factor such as grade 3 hypertension or hypercholesterolaemia • **Severe CKD** (eGFR < 30 mL/min/1.73 m^2) • **A calculated 10 year SCORE of ≥ 10%**
High risk	**People with any of the following:** • **Marked elevation of a single risk factor**, particularly cholesterol > 8 mmol/L (> 310 mg/dL), e.g. familial hypercholesterolaemia or grade 3 hypertension (BP ≥ 180/110 mmHg) • **Most other people with diabetes mellitus** (except some young people with type 1 diabetes mellitus and without major risk factors, who may be at moderate-risk)
	Hypertensive LVH
	Moderate CKD (eGFR 30-59 mL/min/1.73 m^2)
	A calculated 10 year SCORE of 5-10 %
Moderate risk	**People with:** • **A calculated 10 year SCORE of ≥ 1 to <5%** • **Grade 2 hypertension** • **Many middle-aged people belong to this category**
Low risk	**People with:** • **A calculated 10 year SCORE of < 1%**

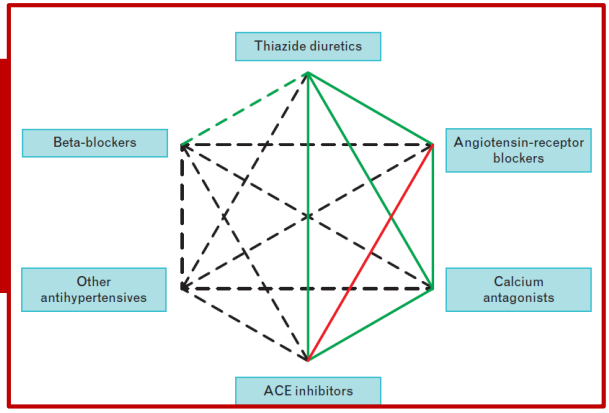
http://www.cardiorisk.fr/

Cibles tensionnelles

Age group	Office SBP treatment target ranges (mmHg)				
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke[a]/TIA
18–65 years	**Target to 130** *or lower if tolerated* Not <120	**Target to 130** *or lower if tolerated* Not <120	**Target to <140 to 130** *if tolerated*	**Target to 130** *or lower if tolerated* Not <120	**Target to 130** *or lower if tolerated* Not <120
65–79 years[b]	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*
≥80 years[b]	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*	**Target to 130–139** *if tolerated*
Office DBP treatment target range (mmHg)	70–79	70–79	70–79	70–79	70–79

- ✓Cibles = range
- ✓TAS ± 130mmHg si toléré sauf si IRC (<140)
- ✓Différences selon âge ≥ 65 ans (TAS<140)
- ✓TAD <80mmHg chez tout le monde

Stratégies thérapeutiques



1 Pill

Initial therapy
Dual combination

ACEi or ARB + CCB or diuretic

Consider monotherapy in low risk grade 1 hypertension (systolic BP <150mmHg), or in very old (≥80 years) or frailer patients

1 Pill

Step 2
Triple combination

ACEi or ARB + CCB + diuretic

2 Pills

Step 3
Triple combination + spironolactone or other drug

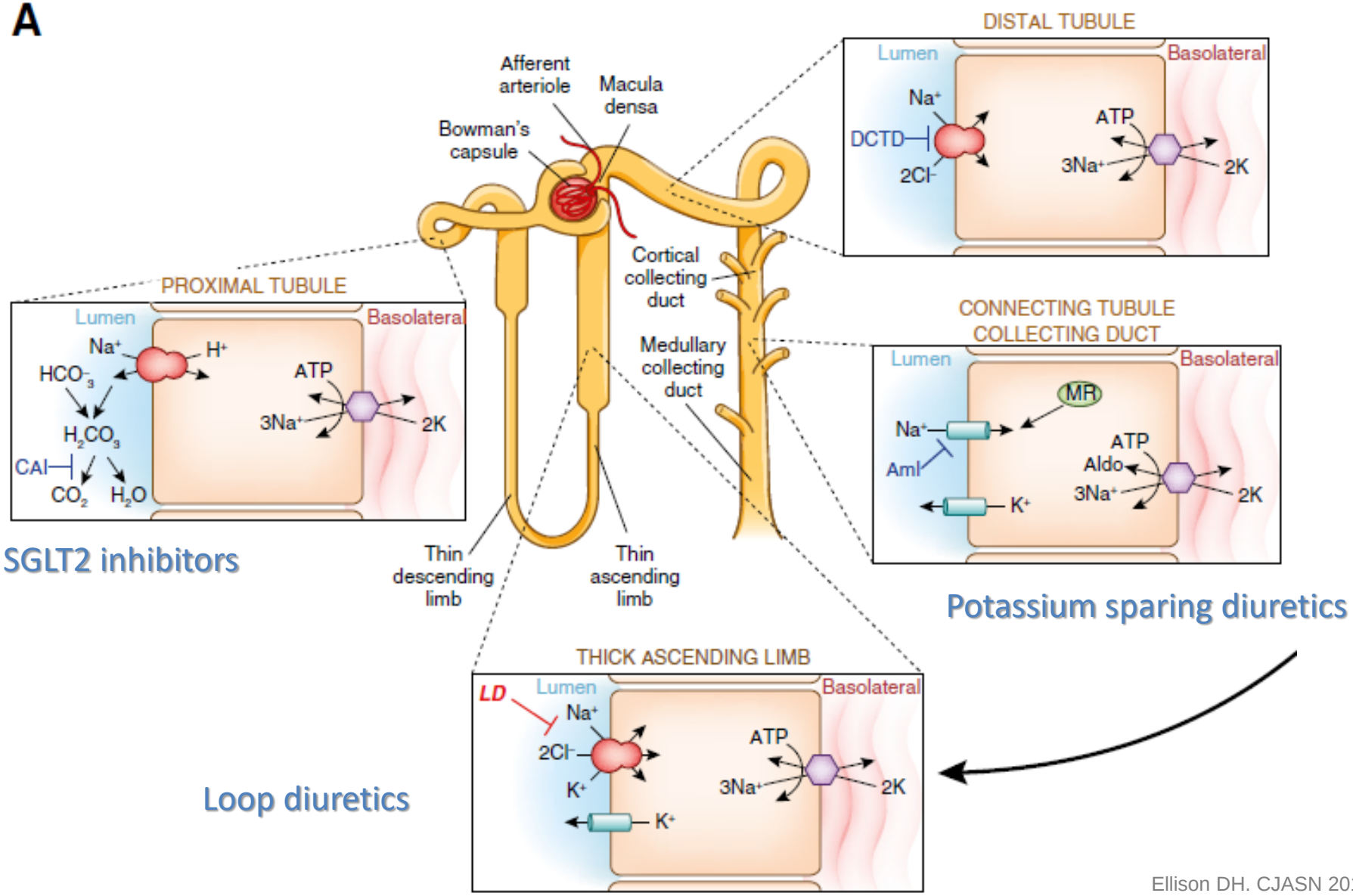
Resistant hypertension
Add spironolactone (25–50 mg o.d.) or other diuretic, alpha-blocker or beta-blocker

Consider referral to a specialist centre for further investigation

Beta-blockers
Consider beta-blockers at any treatment step, when there is a specific indication for their use, e.g. heart failure, angina, post-MI, atrial fibrillation, or younger women with, or planning, pregnancy

Diurétiques - rappel

Thiazide (-like)



SGLT2 inhibitors

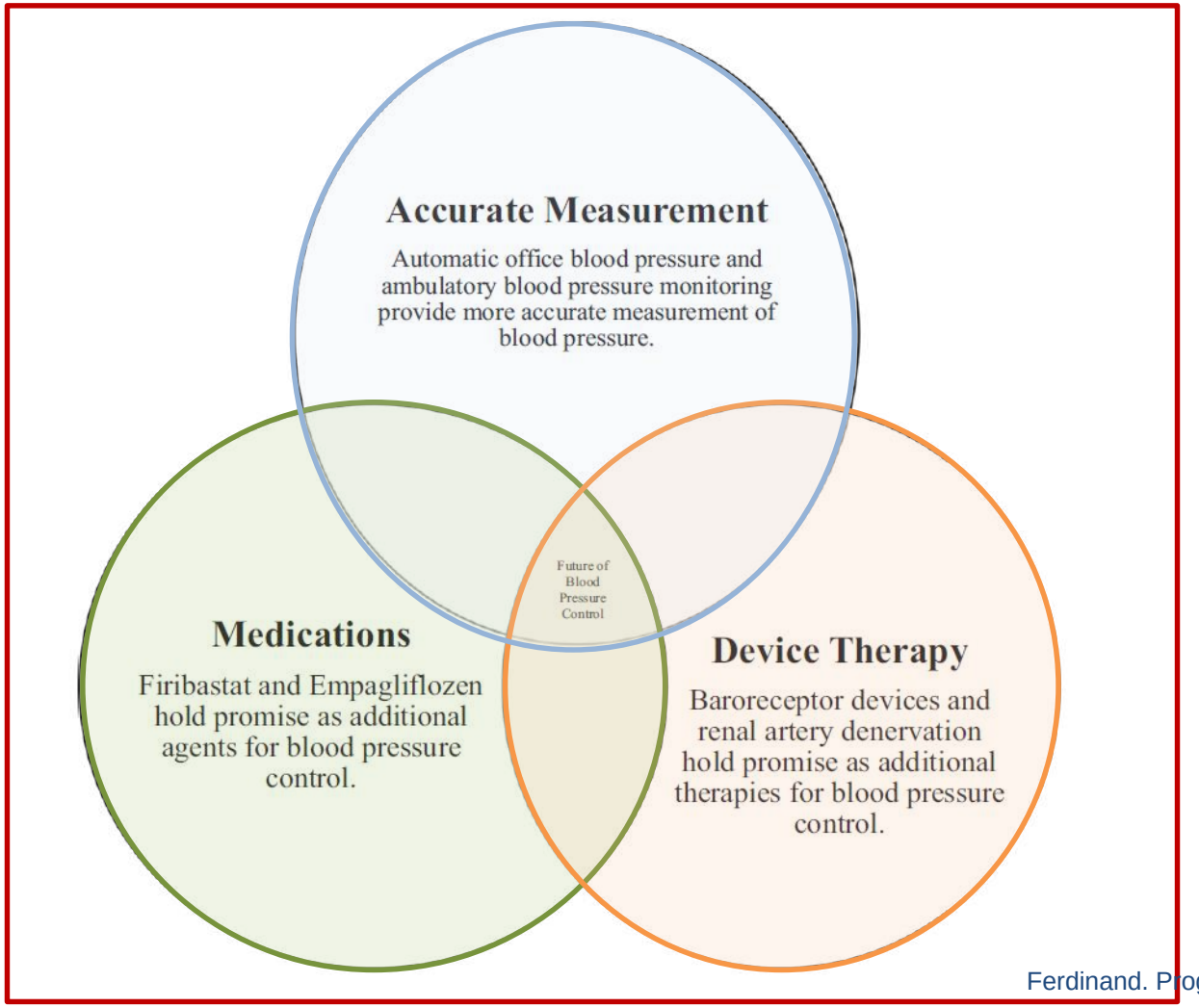
Potassium sparing diuretics

Loop diuretics

Ellison DH. CJASN 2019

Autres stratégies thérapeutiques 2020?

+ Adhérence



Ferdinand. Progress in CV disease 2020

Adhérence en 2020?

3 composants adhérence:

- **Initiation** : 5% études, >20% en Clinique ne commencent pas
- **Implementation**: prend régulièrement dose prescrite (ok si >80%)
- **Arrêt**: 50% à 1 an initiation

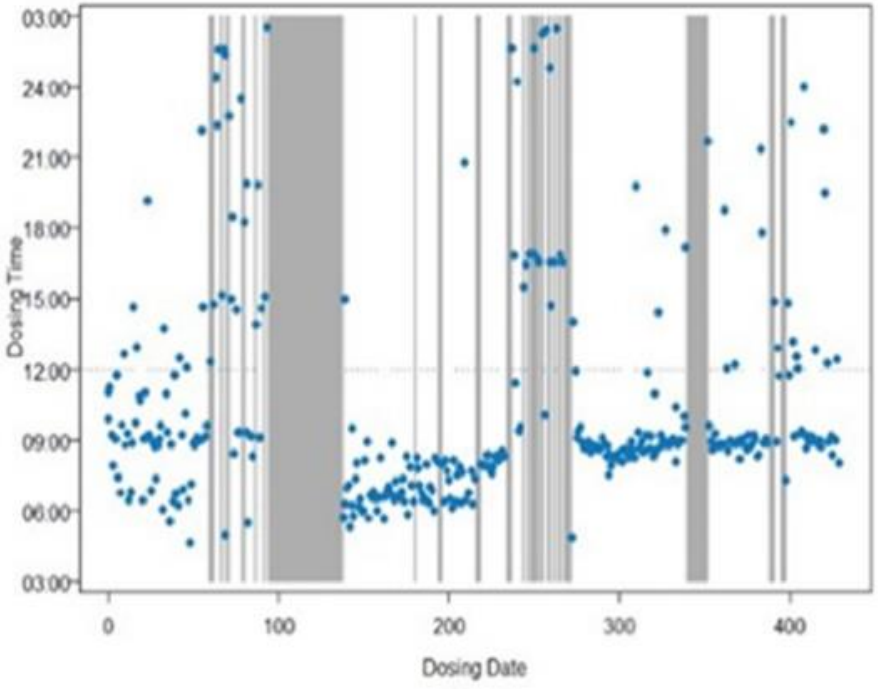
Table 2. Adherence: Five Categories of Factors Impacting Adherence to Prescription Medications*

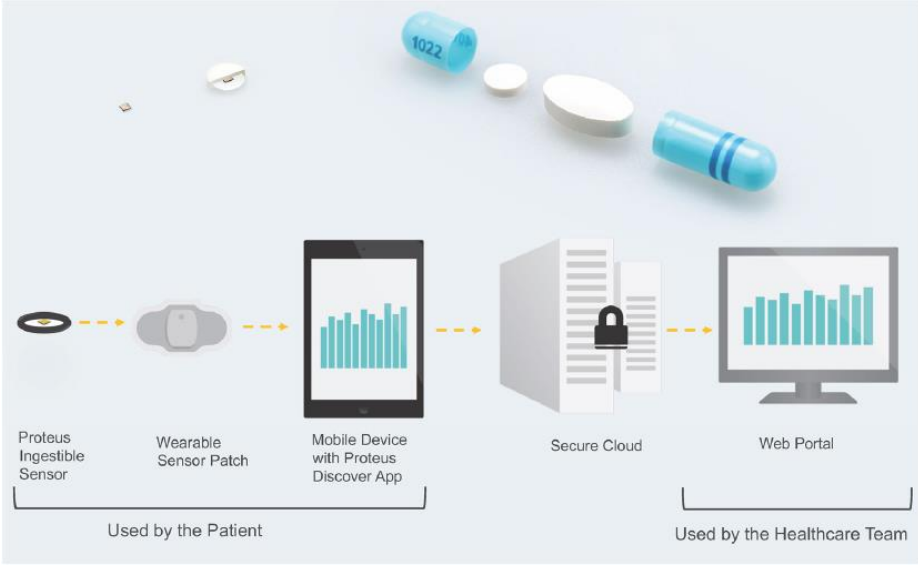
Sociodemographic	Health Care Team/Health Care System	Therapy-Related	Condition-Related	Patient-Related
Young and very old adults	Patient-clinician relationship	Complex regimens	Multiple chronic conditions	Deny diagnosis
Minority race-ethnicity	Communication style	Treatment changes	Depression, psychoses	Perception of illness severity/future impact
Low income, poverty	Patient-centeredness	Treatment failure	Drug/alcohol abuse	Perception of treatment efficacy
Homeless, unstable home	Lack of team-based care	Time to benefit	Dementia	Fear dependence or adverse effects
Social support	Clinician burn out	Adverse effects	Major disability	Lack knowledge/misunderstanding
Copayments	Fail to detect clues	Treatment duration	Symptom severity	Forget
(Health) literacy	Lack knowledge/QI support	Refill frequency	Quality of life	Limited follow-up
Transportation, rural residents	Access to and cost of care	Refill consolidation		Low self-efficacy/discount future
War, disasters	Pay for volume			Alternative therapy

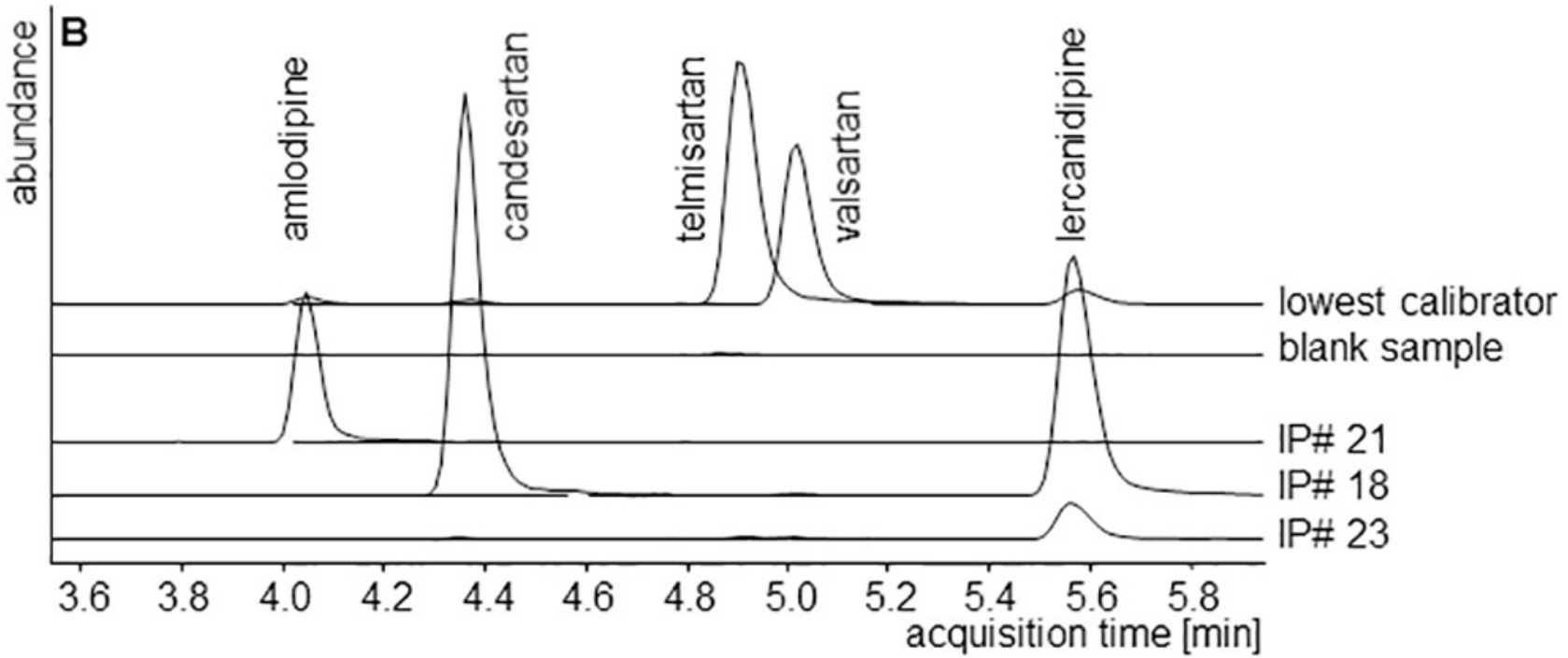
Burnier. Circ Res 2019

Methods	Interview	Questionnaire	Pill Count	Refill Data	DOT	Electronic Monitoring	Drug Assay	Digital Medicine*
Type of data	Qualitative	Qualitative	Quantitative	Quantitative	Quantitative	Quantitative	Qualitative	Quantitative
Reliability	–	–	+	+	+++	+++	+++	+++
Validity	+	+	+	+	+++	+++	+++	+++
Objectivity	–	–	–	+	+++	++	++	+++
Simplicity	+++	+++	++	–	+	+	±	±
Cost	––	–	+	+	+++	++	+++	–?
Availability	+++	+++	++	–	+	+	+	–
Clinical use	+++	+	+	+	++	+	+	–

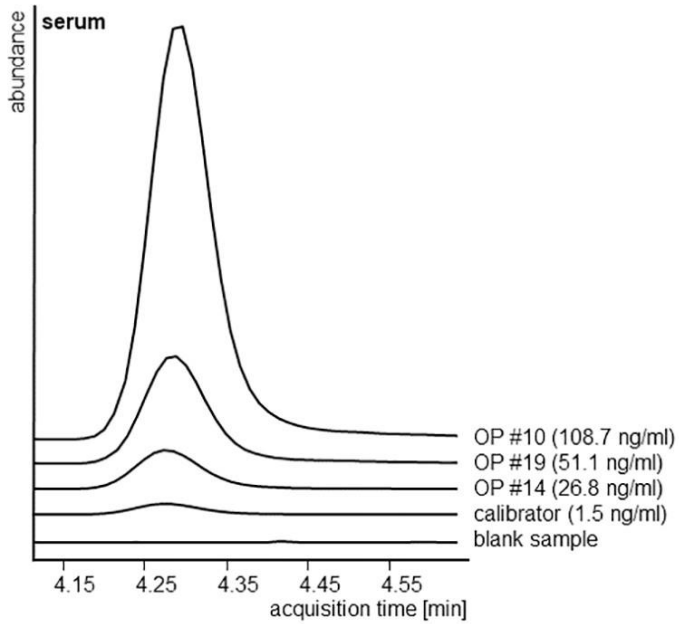
Mesure Adhérence

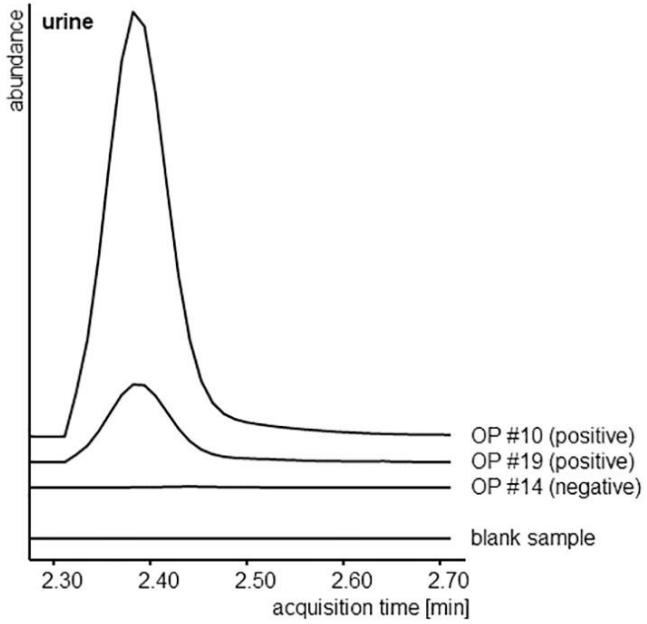




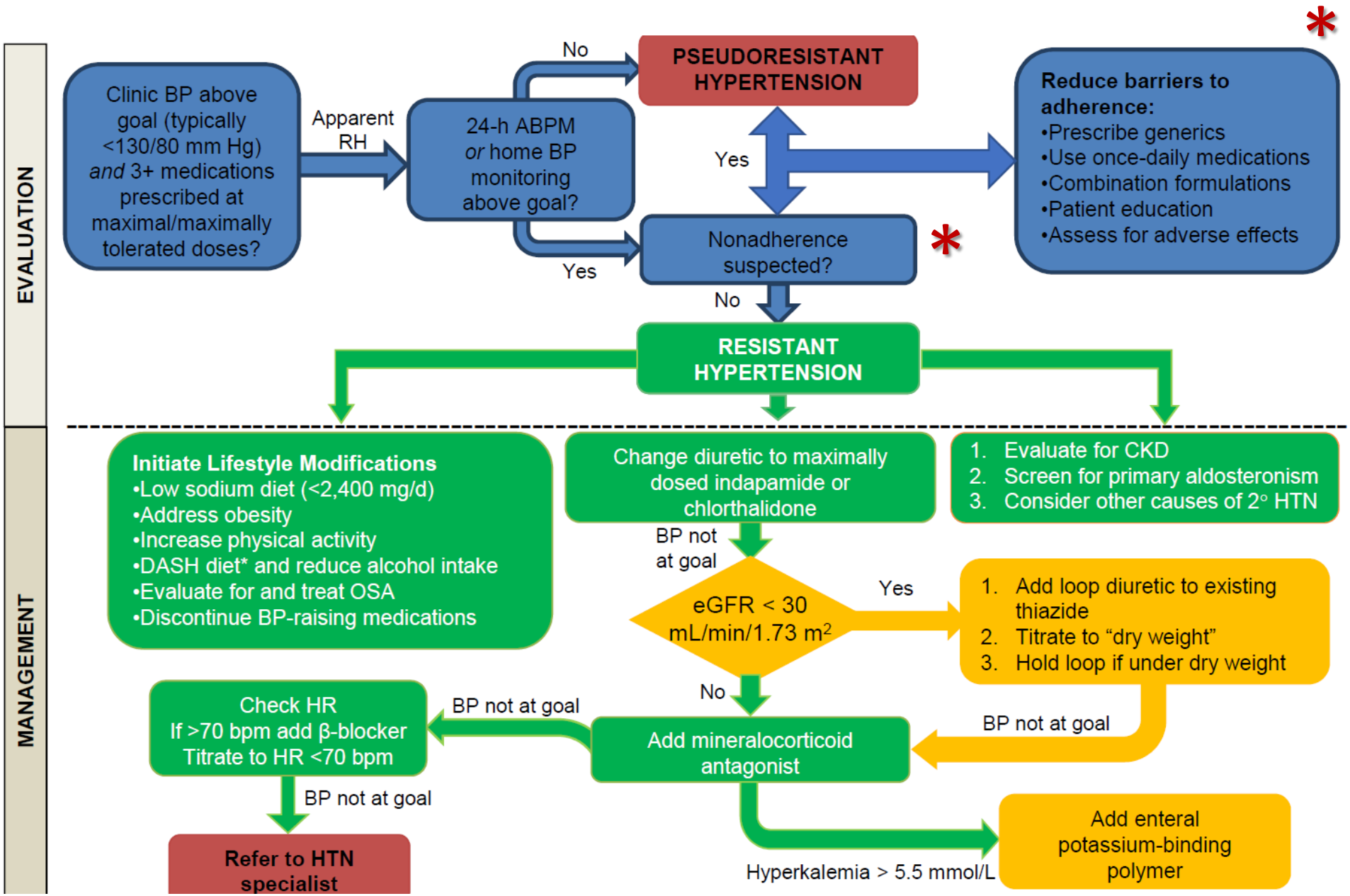


Mesures par chromatographie Sang ou urine



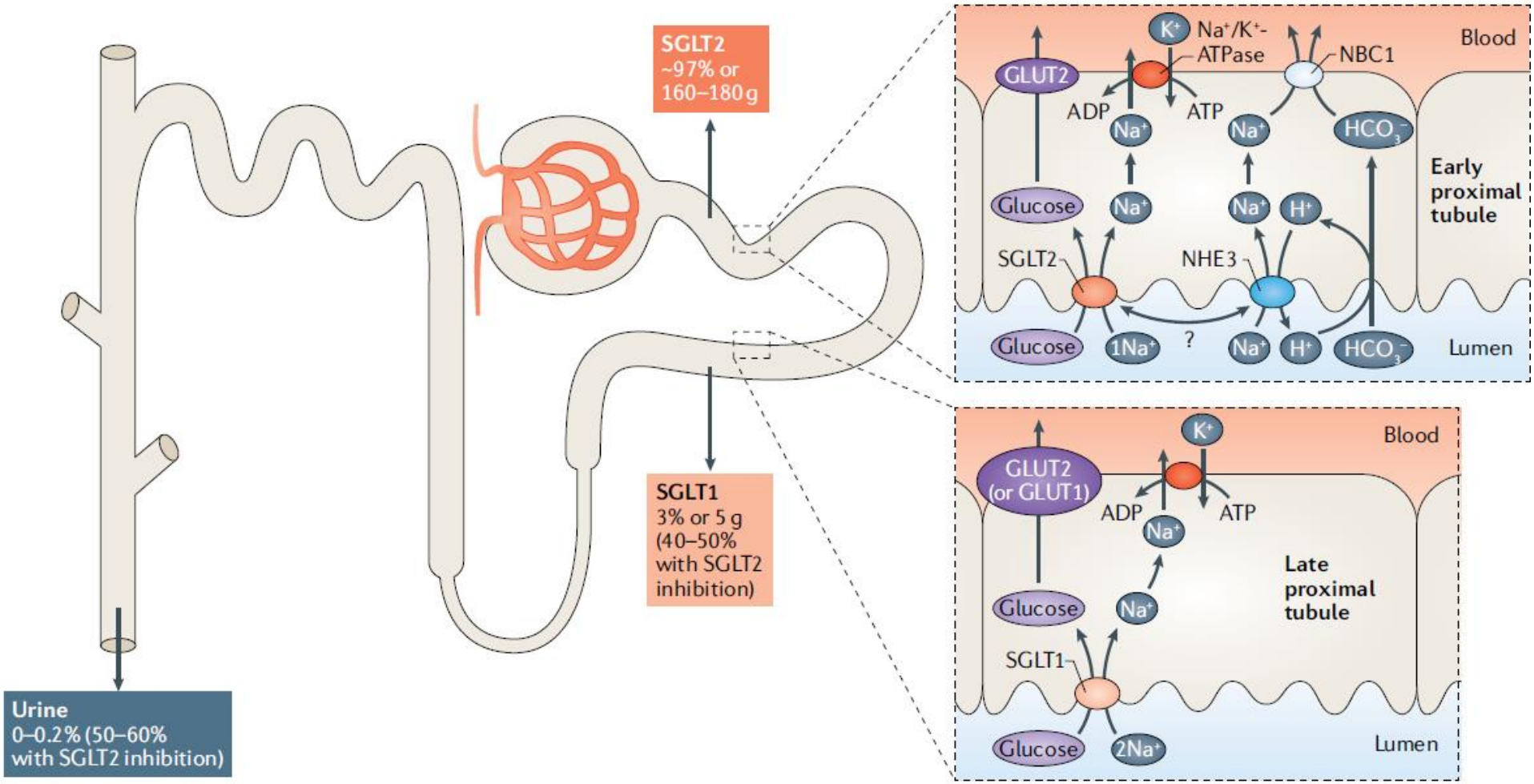


Ritscher . Plos One 2020



Fay KS. AJKF 2020

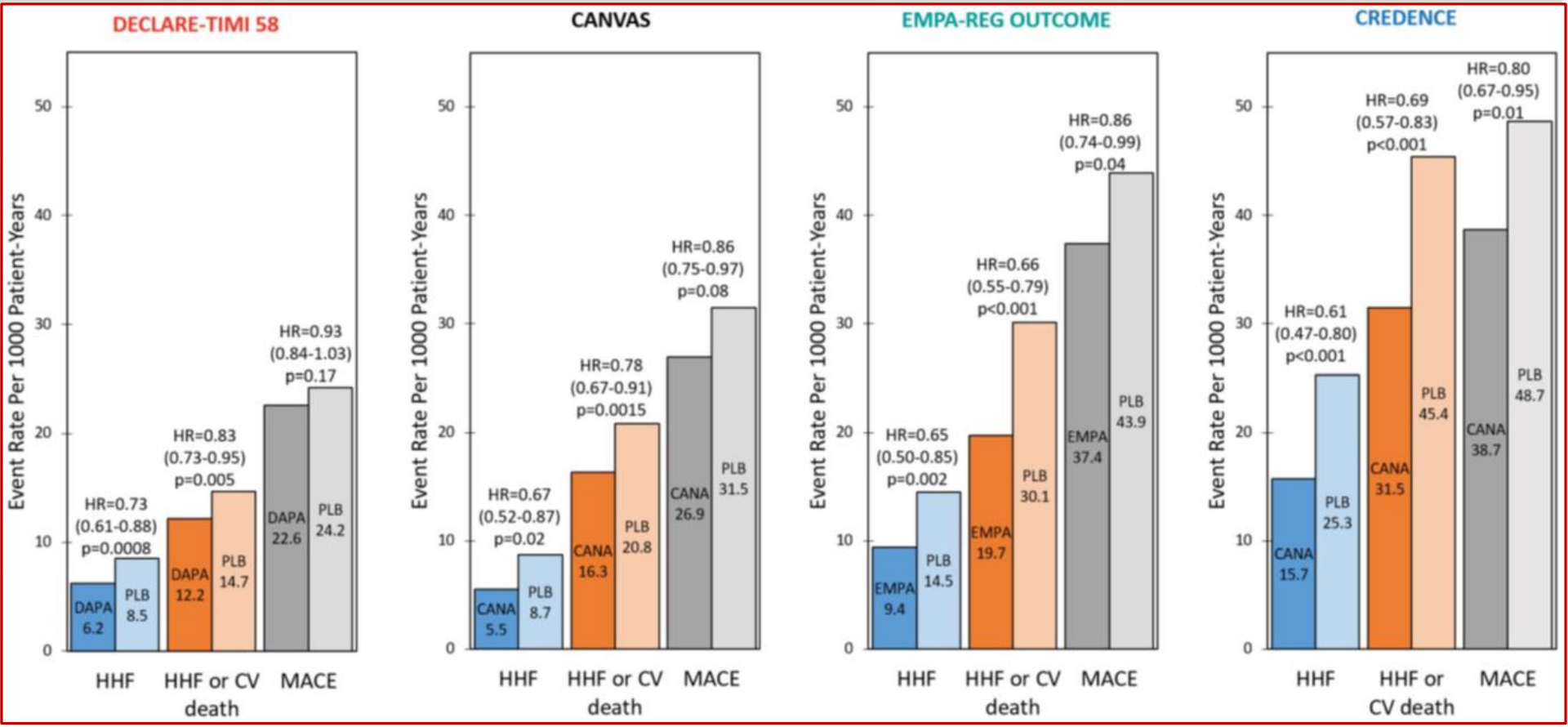
SGLT 2 & inhibiteurs: physiopathologie



Vallon V. Nat Rev Nephrol2020

Trial parameter	EMPA-REG OUTCOME[29]	CANVAS Program[30]	DECLARE-TIMI 58 (REF.[31])	CREDENCE[32]	DAPA-HF[14]
Intervention	Empagliflozin 10 mg or 25 mg versus placebo	Canagliflozin 100 mg or 300 mg versus placebo	Dapagliflozin 10 mg versus placebo	Canagliflozin 100 mg versus placebo	Dapagliflozin 10 mg versus placebo
Population (*n*)	7,020 patients with T2DM and established cardiovascular disease	10,142 patients with T2DM and established cardiovascular disease or ≥2 cardiovascular risk factors	17,160 patients with T2DM and established cardiovascular disease or risk factors for cardiovascular disease	4,401 patients with T2DM and albuminuric chronic kidney disease treated with RAAS blockade	4,744 patients with HFrEF (ejection fraction ≤40%) in NYHA class II–IV (45% with T2DM)
Established cardiovascular disease at baseline (%)	99	66	41	50	100 with HF (56 ischaemic aetiology)
Mean follow-up (years)	3.1	3.6	4.2	2.6	1.5
HbA_{1c} level at baseline	7–10% with stable background therapy or 7–9% for drug-naive patients	7.0–10.5%	6.5–12.0%	6.5–12.0%	No restriction
eGFR (ml/min/1.73 m^2)	≥30	≥30	≥60	30–89	≥30
Primary outcomes	3P MACE (HR 0.86, 95% CI 0.74–0.99)	3P MACE (HR 0.86, 95% CI 0.75–0.97)	3P MACE (HR 0.93, 95% CI 0.84–1.03); cardiovascular death or hospitalization for HF (HR 0.83, 95% CI 0.73–0.95)	New ESRD or doubling of serum creatinine level or renal or cardiovascular death (HR 0.66, 95% CI 0.53–0.81)	Hospitalization for HF or cardiovascular death, including urgent hospital visit with intravenous therapy for HF (HR 0.74, 95% CI 0.65–0.85)
Cardiovascular death	HR 0.62, 95% CI 0.49–0.77	HR 0.87, 95% CI 0.72–1.06	HR 0.98, 95% CI 0.82–1.17	HR 0.78, 95% CI 0.61–1.00	HR 0.82, 95% CI 0.69–0.98
All-cause mortality	HR 0.68, 95% CI 0.57–0.82	HR 0.87, 95% CI 0.74–1.01	HR 0.93, 95% CI 0.82–1.04	HR 0.83, 95% CI 0.68–1.02	HR 0.83, 95% CI 0.71–0.97

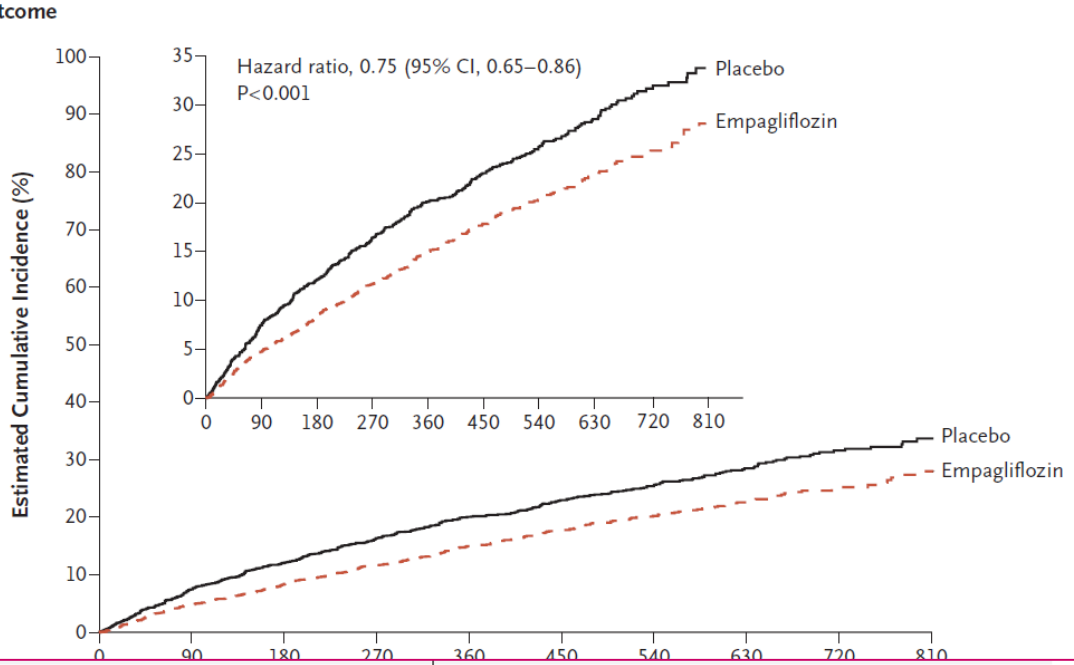
Trial parameter	EMPA-REG OUTCOME[29]	CANVAS Program[30]	DECLARE-TIMI 58 (REF.[31])	CREDENCE[32]	DAPA-HF[14]
Intervention	Empagliflozin 10 mg or 25 mg versus placebo	Canagliflozin 100 mg or 300 mg versus placebo	Dapagliflozin 10 mg versus placebo	Canagliflozin 100 mg versus placebo	Dapagliflozin 10 mg versus placebo
Population (*n*)	7,020 patients with T2DM and established cardiovascular disease	10,142 patients with T2DM and established cardiovascular disease or ≥2 cardiovascular risk factors	17,160 patients with T2DM and established cardiovascular disease or risk factors for cardiovascular disease	4,401 patients with T2DM and albuminuric chronic kidney disease treated with RAAS blockade	4,744 patients with HFrEF (ejection fraction ≤40%) in NYHA class II–IV (45% with T2DM)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure



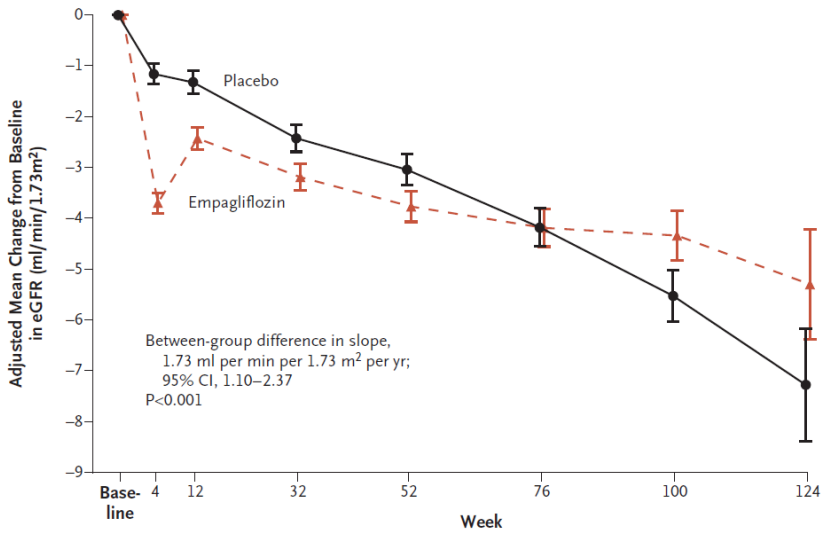
Baseline diabetes status				
Diabetes	200/927	265/929		0.72 (0.60–0.87)
No diabetes	161/936	197/938		0.78 (0.64–0.97)

METHODS

In this double-blind trial, we randomly assigned 3730 patients with class II, III, or IV heart failure and an ejection fraction of 40% or less to receive empagliflozin (10 mg once daily) or placebo, in addition to recommended therapy. The primary outcome was a composite of cardiovascular death or hospitalization for worsening heart failure.

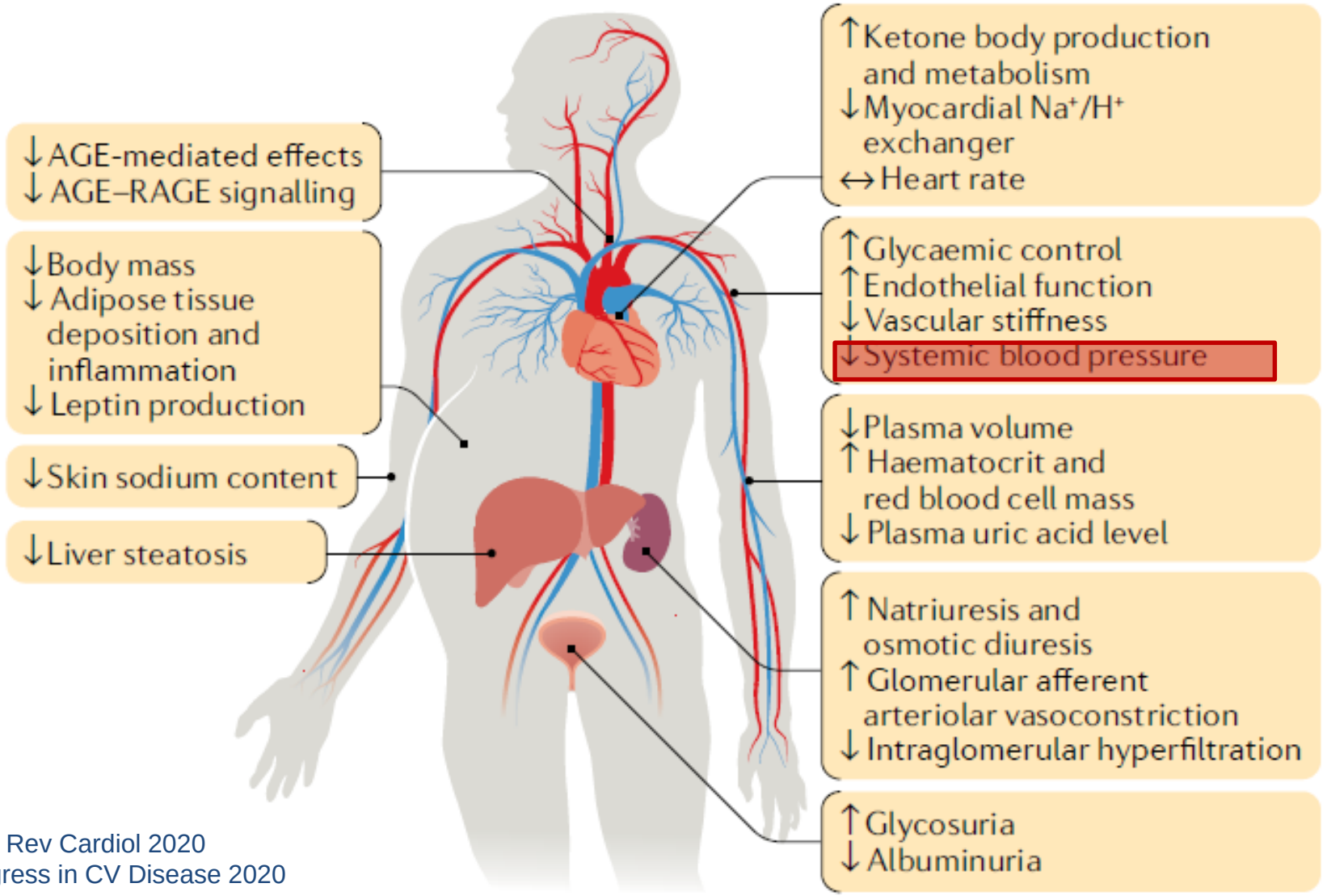
RESULTS

During a median of 16 months, a primary outcome event occurred in 361 of 1863 patients (19.4%) in the empagliflozin group and in 462 of 1867 patients (24.7%) in the placebo group (hazard ratio for cardiovascular death or hospitalization for heart failure, 0.75; 95% confidence interval [CI], 0.65 to 0.86; P<0.001). The effect of empagliflozin on the primary outcome was consistent in patients regardless of the presence or absence of diabetes. The total number of hospitalizations for heart failure was lower in the empagliflozin group than in the placebo group (hazard ratio, 0.70; 95% CI, 0.58 to 0.85; P<0.001). The annual rate of decline in the estimated glomerular filtration rate was slower in the empagliflozin group than in the placebo group (–0.55 vs. –2.28 ml per minute per 1.73 m^2 of body-surface area per year, P<0.001), and empagliflozin-treated patients had a lower risk of serious renal outcomes. Uncomplicated genital tract infection was reported more frequently with empagliflozin.



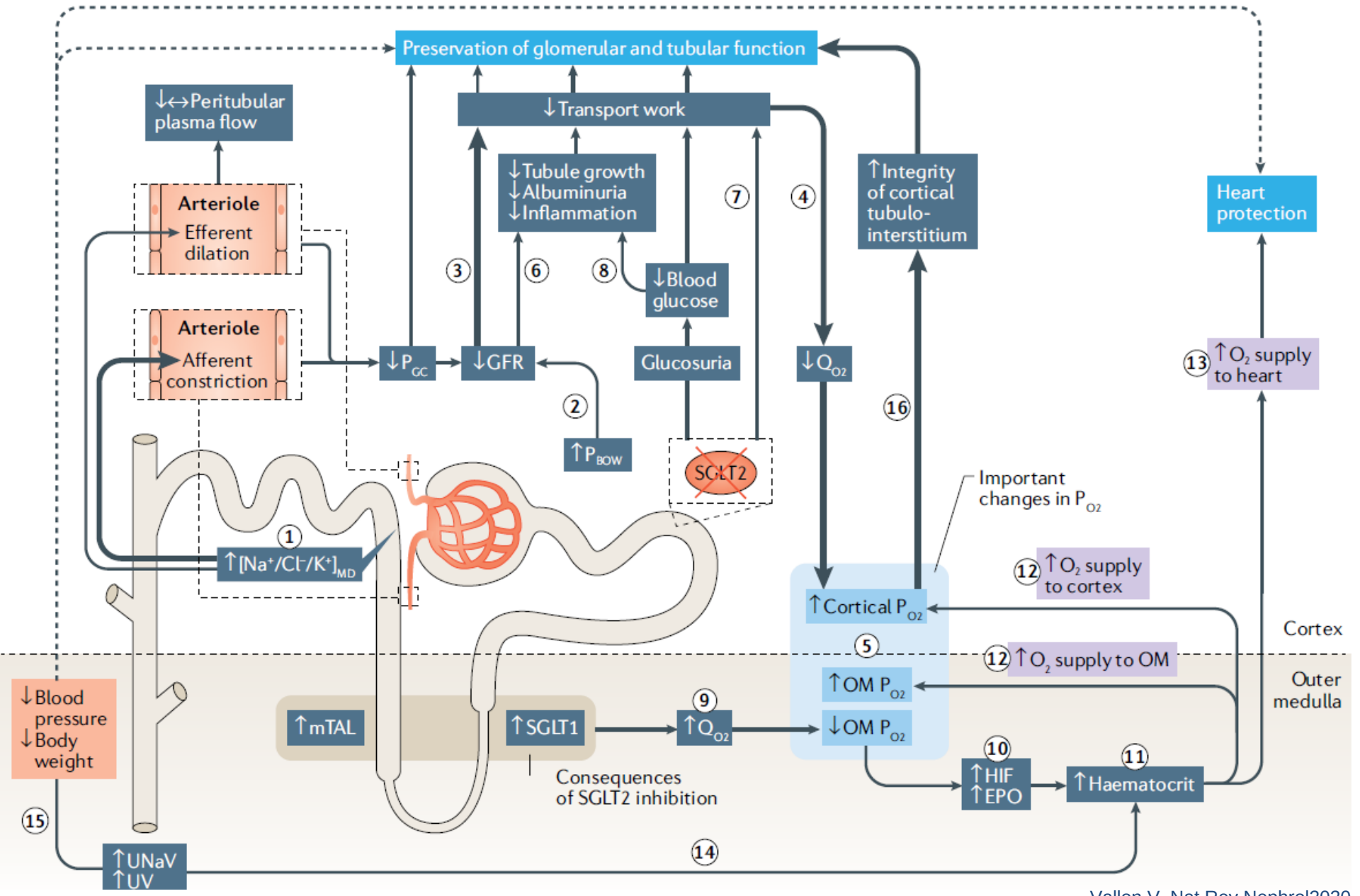
No. at Risk								
Placebo	1792	1765	1683	1500	1146	745	343	76
Empagliflozin	1799	1782	1720	1554	1166	753	356	80

SGLT 2 inhibiteurs: effets bénéfiques



Cowie. Nat Rev Cardiol 2020
Kario. Progress in CV Disease 2020

Conséquences rénales inhibition SGLT2



Vallon V. Nat Rev Nephrol2020

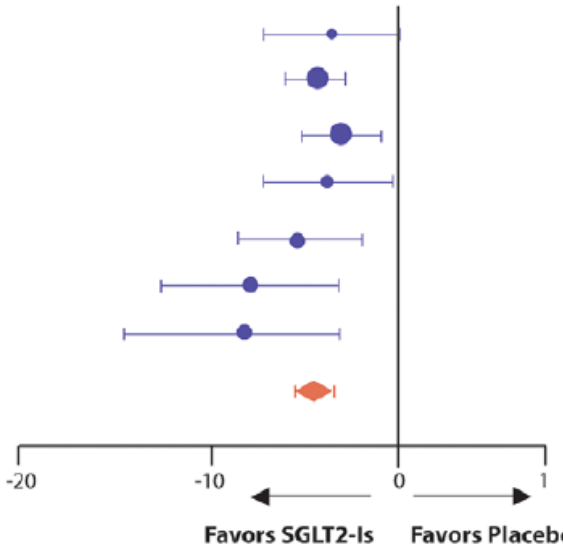
SGLT 2 inhibiteurs: effects sur PA

Study	*N*	HTN, *n* (%)	Drug (vs. comparator)	Office BP		24-h ABP	
				SBP	DBP	SBP	DBP
EMPA-REG trial [10]	7020	6667 (95)	Empagliflozin (vs. PL)	4.0	1.5		
EMPA-REG BP [11]	547	547 (100)	Empagliflozin 10 mg (vs. PL)	3.9	1.9	3.4	1.4
EMPA-REG BP [11]	547	547 (100)	Empagliflozin 25 mg (vs. PL)	4.8	1.9	4.2	1.7
Mancia et al. [12]	547	547 (100)	Empagliflozin 10 mg (vs. PL)			2.4–4.7	0.7–2.6
Mancia et al. [12]	547	547 (100)	Empagliflozin 25 mg (vs. PL)			3.8–4.3	1.5–2.5
SACRA trial [13]	132	132 (100)	Empagliflozin 10 mg (vs. PL)	8.6	2.0	7.7	2.9
Mazidi et al. [26][a]	2106	NA	Empagliflozin (vs. PL)	2.6	1.1		
Liakos et al. [28][a]	6203	NA	Empagliflozin (vs. PL)	4.0	2.0		
DECLARE-TIMI 58 [14]	17,160	NA	Dapagliflozin 10 mg (vs. PL)	2.7	0.7		
DAPA-HF trial [3]	4744	3510 (74)	Dapagliflozin 10 mg (vs. PL)	1.3			
Sjostrom et al. [15]	4516	1293 (29)	Dapagliflozin 10 mg (vs. PL)	2.6–3.6	1.2		
Weber et al. [16]	613	613 (100)	Dapagliflozin 10 mg (vs. PL)	3.1		2.9	
Weber et al. [17]	449	449 (100)	Dapagliflozin 10 mg (vs. PL)	4.3			
Shah et al. [18]	NA	NA	Dapagliflozin (vs. PL)	2.5–5.0	1.5–3.0		
Mazidi et al. [26][a]	8570	NA	Dapagliflozin (vs. comparators)	1.0	0.7		
CANVAS Program [20]	10,142	9125 (90)	Canagliflozin (vs. PL)	3.9	1.4		
Townsend et al. [21]	113	113 (100)	Canagliflozin 100 mg (vs. PL)	1.3	-0.2	3.3	1.9
	112	112 (100)	Canagliflozin 300 mg (vs. PL)	3.6	0.6	4.9	2.9
Mazidi et al. [26][a]	9053	NA	Canagliflozin (vs. comparators)	2.2	2.2		
Baker et al. [29][a]	169	169 (100)	Canagliflozin (vs. PL)			4.7	2.4

SGLT 2 inhibiteurs: effects sur PA

Author	SGLT2-Is		Placebo		ΔΔ (95% CI)	SBP, mm Hg	P
	No.	Δ (SD)	No.	Δ (SD)			
Lambers Heerspink, 2013	24	-5.6 (11.6)	25	-0.7 (9.2)	-3.3 (-6.8, 0.2)		0.07
Tikkanen, 2015	276	-3.7 (8.3)	271	0.5 (8.2)	-4.2 (-5.5, -2.8)		<0.001
Weber, 2015	267	-9.6 (20.0)	263	-6.7 (20.3)	-2.9 (-4.9, -0.9)		0.004
Amin, 2015	36	-3.5 (7.0)	36	0.1 (6.6)	-3.6 (-6.9, -0.3)		0.03
Townsend, 2016	56	-6.2 (10.5)	56	-1.2 (10.5)	-4.9 (-8.4, -1.5)		0.006
Kario, 2018	68	-10.0 (14.1)	63	-2.4 (14.0)	-7.7 (-12.5, -2.8)		0.002
Ferdinand, 2019	78	-10.3 (16.3)	72	-1.9 (16.5)	-8.4 (-13.7, -3.0)		0.003
Total	805		786		-4.4 (-5.5, -3.4)		<0.001

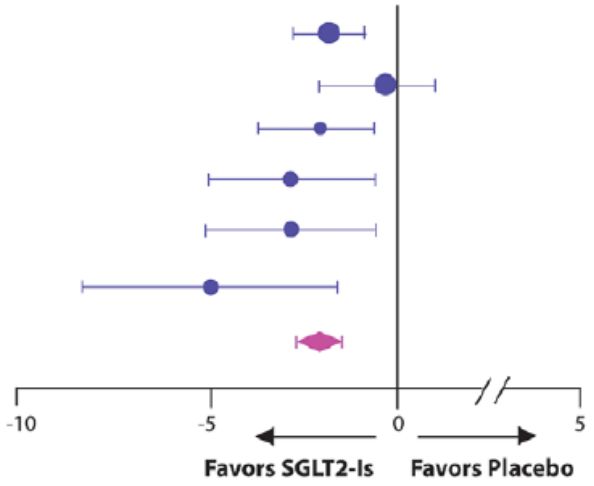
Heterogeneity (Q=5.10, I^2= 0.0%, P=0.53)



B

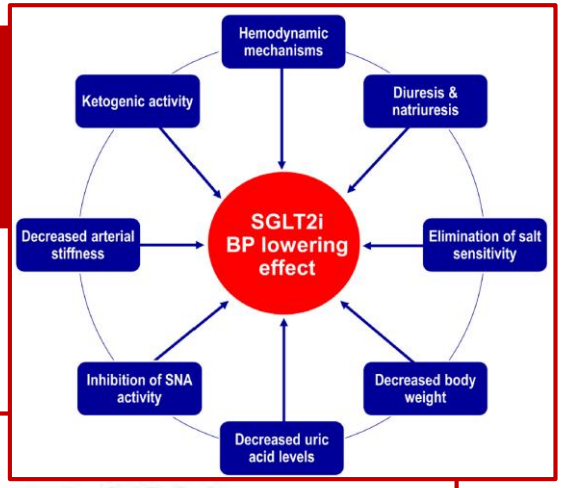
Author	SGLT2-Is		Placebo		ΔΔ (95% CI)	DBP, mm Hg	P
	N°	Δ (SD)	N°	Δ (SD)			
Tikkanen, 2015	276	-1.4 (5.3)	271	0.3 (5.1)	-1.7 (-2.5, -0.9)		<0.001
Weber, 2015	267	-6.2 (13.8)	263	-5.5 (13.7)	-0.6 (-2.0, 0.7)		0.38
Amin, 2015	36	-1.5 (4.7)	36	0.8 (4.7)	-2.2 (-3.6, -0.8)		0.002
Townsend, 2016	56	-3.2 (6.0)	56	-0.3 (6.0)	-2.9 (-5.0, -0.9)		0.005
Kario, 2018	68	-3.5 (6.1)	63	-0.7 (6.1)	-2.9 (-5.0, -0.8)		0.008
Ferdinand, 2019	78	-5.0 (11.7)	72	-2.6 (11.3)	-4.9 (-8.4, -1.5)		0.006
Total	781		761		-1.9 (-2.6, -1.2)		<0.001

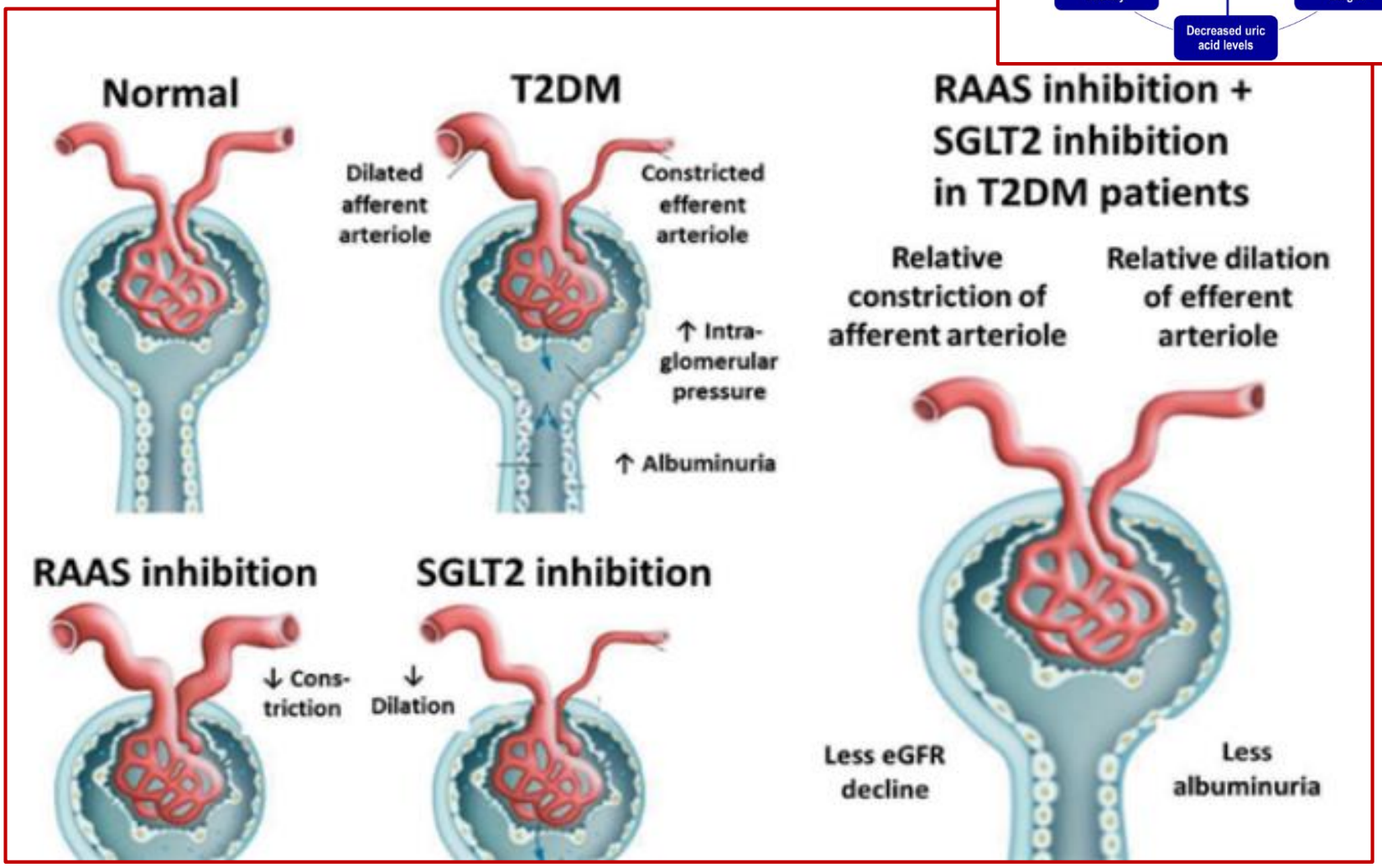
Heterogeneity (Q=2.90, I^2=0.0%, P=0.72)



Meta-analysis. Hypertension 2020

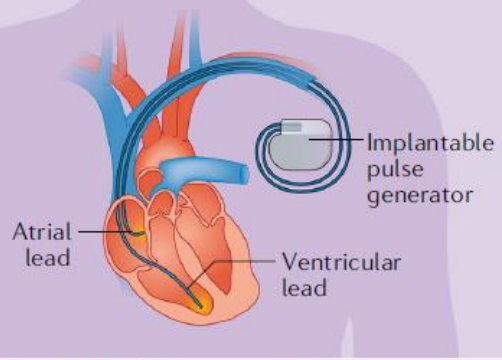
Effet additif IECA/ARA2 et SGLT2i





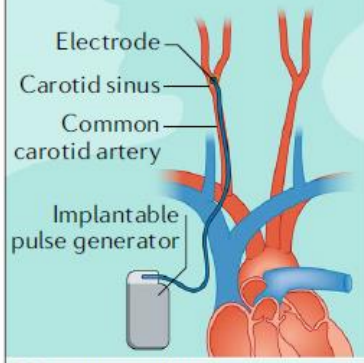
Device therapy….

Cardiac neuromodulation therapy

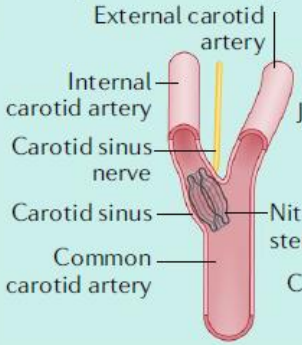


Short-term safety	✓
Long-term safety	?
Short-term efficacy	✓
Long-term efficacy	?

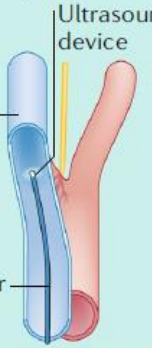
Electrical baroreflex activation therapy



Endovascular baroreflex amplification therapy

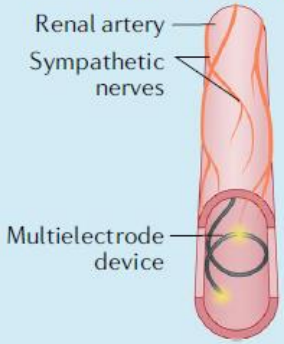


Transvenous carotid body ablation

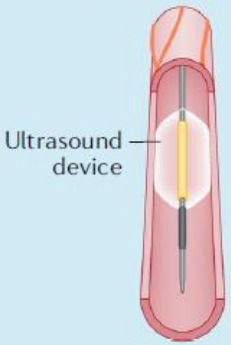


Short-term safety	✗	?	?
Long-term safety	?	?	?
Short-term efficacy	✓	?	?
Long-term efficacy	?	?	?

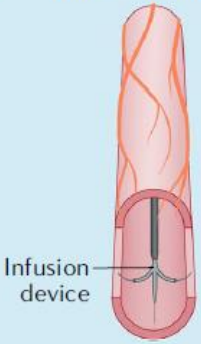
*** Radiofrequency-based renal denervation



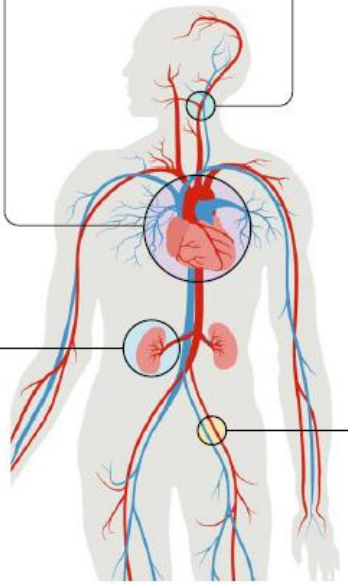
Ultrasound-based renal denervation



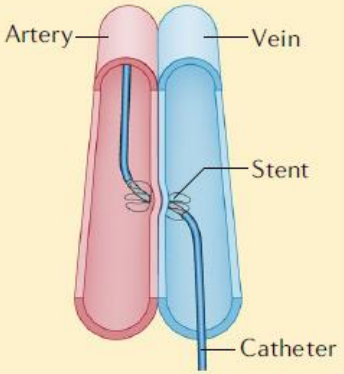
Alcohol-mediated renal denervation



Short-term safety	✓	✓	✓
Long-term safety	✓	?	?
Short-term efficacy	✓	✓	?
Long-term efficacy	?	?	?

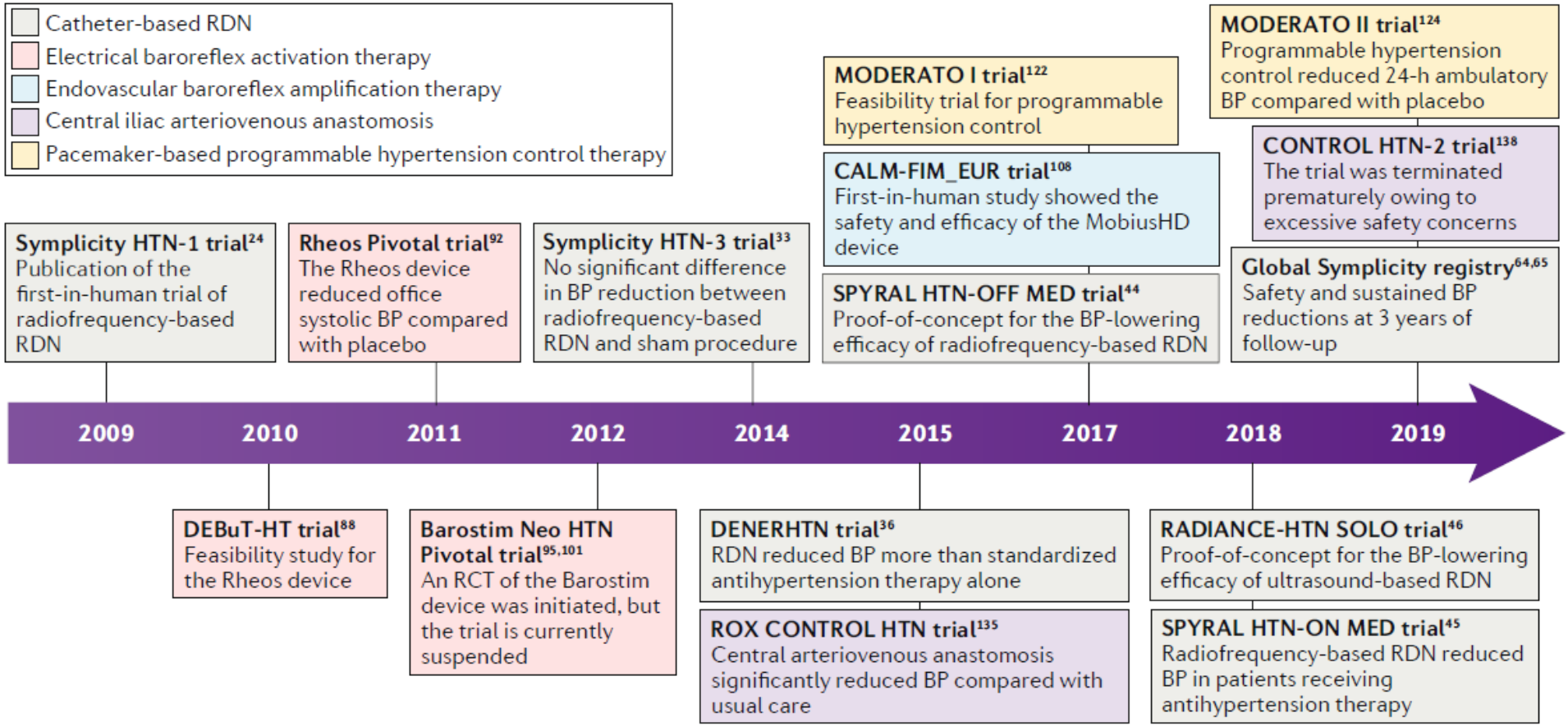


Central iliac arteriovenous coupler



Short-term safety	✗
Long-term safety	✗
Short-term efficacy	✓
Long-term efficacy	?

Device therapy history….



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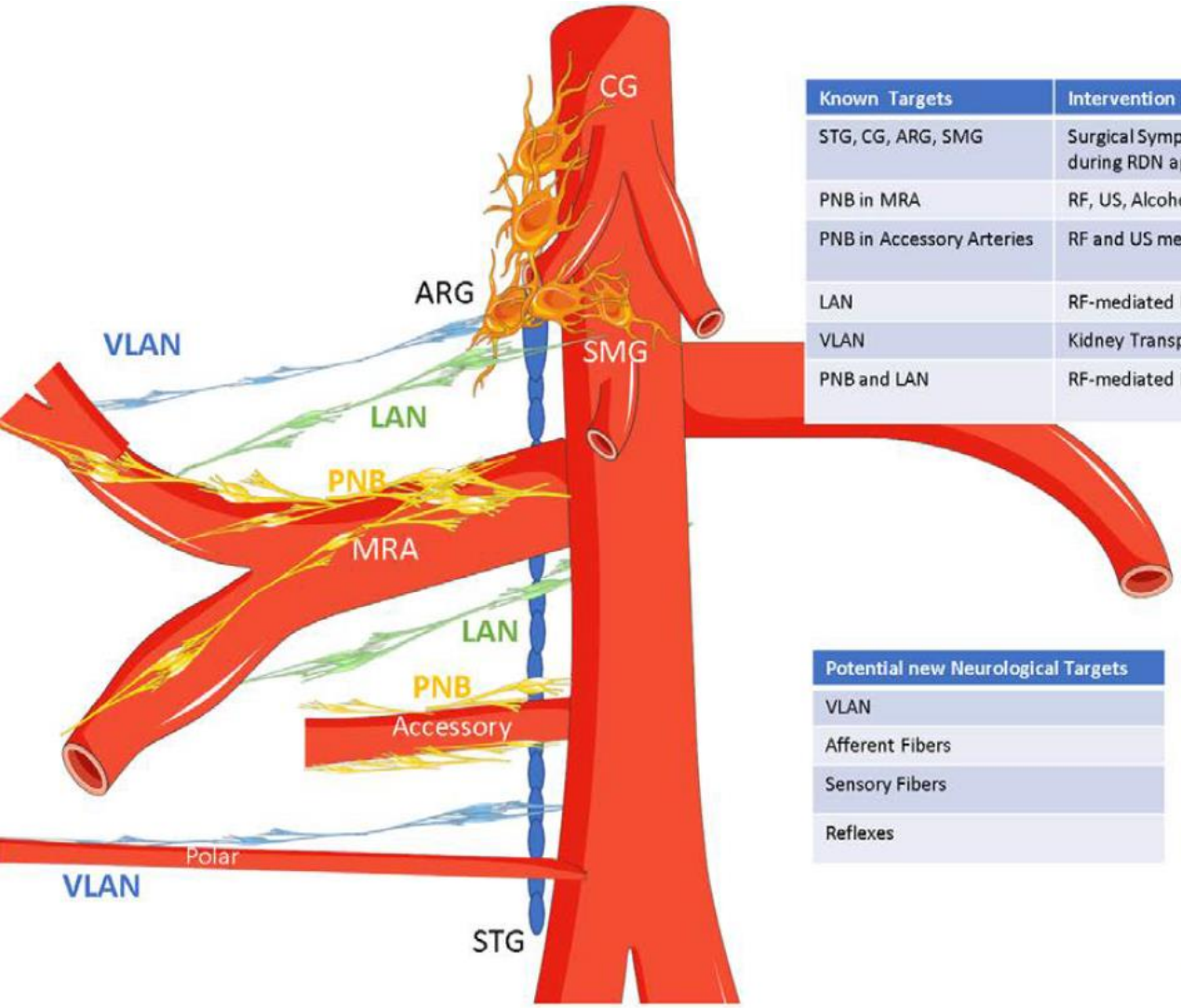
Le retour de la dénervation rénale…



Known Targets	Intervention	Comment
STG, CG, ARG, SMG	Surgical Sympathectomy. Possibly also during RDN applied at the ostium of MRA	Possible lesions of PNB during surgical procedures.
PNB in MRA	RF, US, Alcohol-mediated RDN	
PNB in Accessory Arteries	RF and US mediated RDN	According to arterial diameter, still debatable
LAN	RF-mediated RDN	
VLAN	Kidney Transplant	Purely hypothetical
PNB and LAN	RF-mediated RDN	No difference with US mediated RDN in MRA

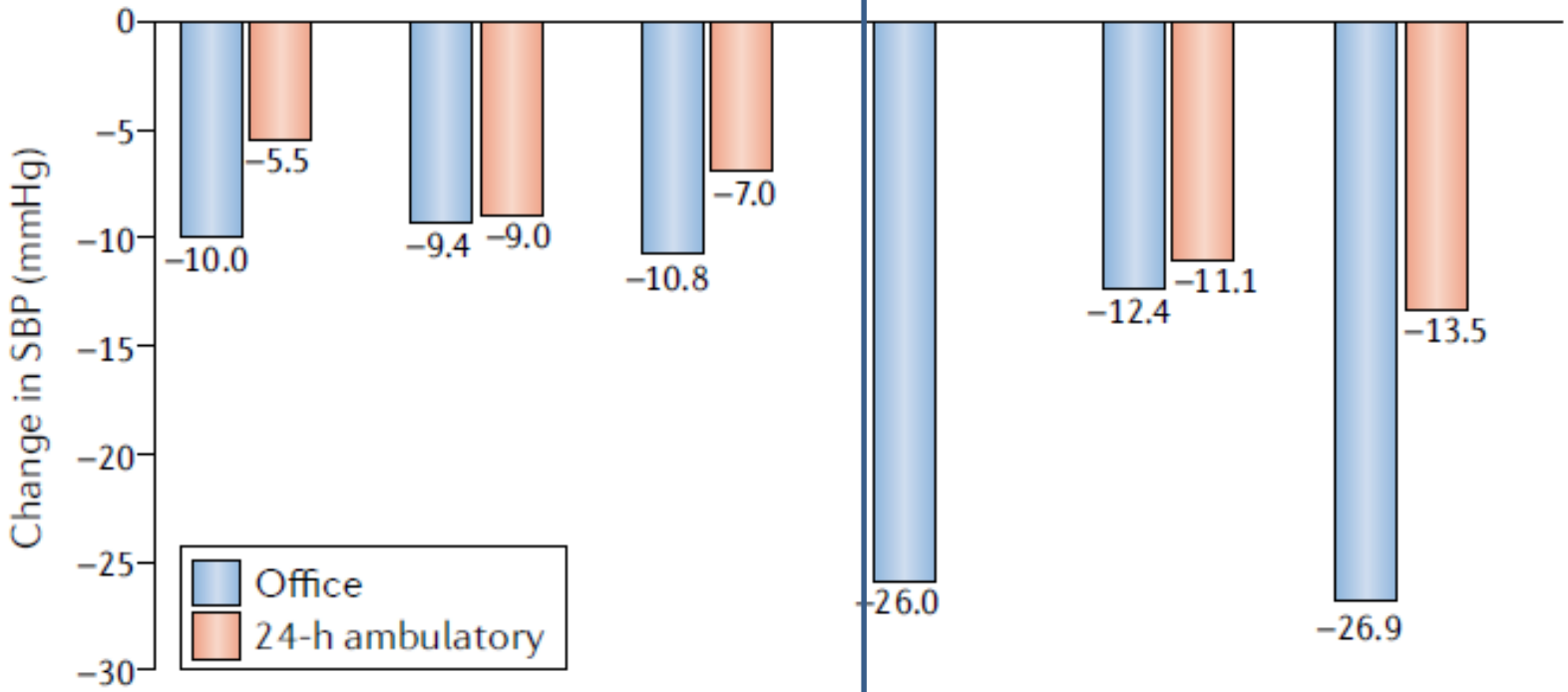
Potential new Neurological Targets
VLAN
Afferent Fibers
Sensory Fibers
Reflexes

Factors modulating RDN impact on innervation
Reflexes (reno-renal, mecano-, metabo- , baro-, chemo- reflexes)
Developmental aspects
Neurohumoral aspects (catecholamine metabolism, receptor status)
Involvement of other hormones (angiotensin 2) , peptides (CGRP, NPY, VIP) or non-neural mediators (NO, prostaglandins)
Status of Intracellular pathways
Anatomical or functional reinnervation

Garcia Touchard. Hypertension 2020

Device therapy: efficacité…

	SPYRAL HTN-OFF MED[a]	SPYRAL HTN-ON MED[a]	RADIANCE-HTN SOLO[a]	Rheos Pivotal	MODERATO II[a]	ROX CONTROL-HTN
Follow-up (months)	3	6	2	6	6	6
Number of patients	35	36	74	170	26	42



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Mme C – 65 ans

Patiente avec IRC stade 3bA1 (eGFR 40ml/min et albU<30mg/g)

- Diabète type 2 NIR – Hb A1c 8.0%
- HTA traitée depuis 10 ans

TA fluctuantes à domicile: 120/80 → 200/100mmHg

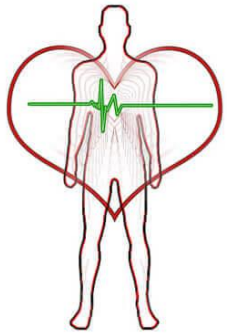
TTT: lisinopril 20mg, carvedilol 12.5mg 2x/j
metformine 1g 2x/j

Status: TA G 127/74mmHg. TA D
poids 70kg pour 1m60 (B

Moyenne 133 /86mmHg
Jour: 134/80mmHg
Nuit: 138 /84mmHg
HT nocturne
Absence de rythme circadien
Variabilité +++

CONCLUSIONS

- ✓ HTA = maladie prévalente, mortalité++
- ✓ Définitions HTA inchangées en Europe
- ✓ Traitement moins conservateur chez ≥ 65 ans
- ✓ Ne pas stopper le tt pour en raison de l'âge mais adapter selon tolérance
- ✓ Importante de contrôle TA ambulatoire



CONCLUSIONS

- ✓ Evidences + faibles pour cibles très basses dans: CAD, âgé, CKD, DM
- ✓ Problème: MAPA et cibles de traitement? Cible office 130mmHg == 125mmHg MAPA…
- ✓ Privilégier traitement combiné → Adhérence
- ✓ Nouveautés: SGLT2 +++ pas que pour DM
- ✓ Devices?

15ème Journée d'Hypertension Romande

1er octobre 2020, de 13h00 à 17h00

Transports publics
Bus: depuis la Gare CFF, Ligne n° 1 (direction Blécherette), changer à Georgette, puis ligne n° 8 (direction Paudex-Verrière), jusqu'à l'arrêt Tour Haldimand.
M2: Gare CFF direction Ouchy
À pied: depuis Ouchy environ 20 minutes, le long du lac

Centre Général Guisan
Rencontre & Culture
Avenue Général-Guisan 117-119
1009 Pully

Questions et inscriptions
Service de Néphrologie | Mme Evelyne Mischler
Tél: +41 21 314 11 54 | Fax: +41 21 314 11 39
E-mail: evelyne.mischler@chuv.ch

13:00	Accueil
13:15	Vieillissement vasculaire: quelle importance dans la prise en charge de l'hypertension? Pr Pierre Boutouyrie, Paris
14:00	Cas clinique «Atteinte vasculaire et Covid-19» Dre Belén Ponte
14:10	Covid-19, hypertension, bloqueurs du SRAA: qu'avons-nous appris? Pr A. Pechère-Bertschi
14:40	Cas clinique hyperaldostéronisme primaire Dre Erietta Polychronopoulou
14:50	Hyperaldostéronisme primaire: update Dr Grégoire Würzner
15:20	Pause
15:40	Cas clinique inhibiteurs des SGLT-2 Dr Karim Gariani
15:50	Les inhibiteurs des SGLT-2 sont-ils les nouveaux antihypertenseurs? Dre Belén Ponte
16:20	Sommeil et hypertension: au-delà du SAOS Pr Raphael Heinzer

Formation continue essentielle
3 crédits: Société Suisse de Cardiologie (SSC)
3 crédits: Société Suisse de Néphrologie (SSN)
3 crédits: Société Suisse d'Angiologie (SSA)
4 crédits: Société Suisse de Médecine interne Générale (SSMIG)