Inserm
La science pour la santé
From science to health

C2VN
Centre de Recherche en CardioVasculaire et Nutrition

Aix*Marseille université
Initiative d'excellence

Hypertension artérielle et maladie rénale chronique

Confluence of interest

VIEWPOINT

Confluence, Not Conflict of Interest
Name Change Necessary

JAMA. 2015;314(17):1791-1792

- Otsuka
- Fresenius Kabi
- Gambro
- BMS
- Astra-Zeneca
- Bayer
- Je travaille sur les toxines urémiques

Ce dont je ne vous parlerai pas

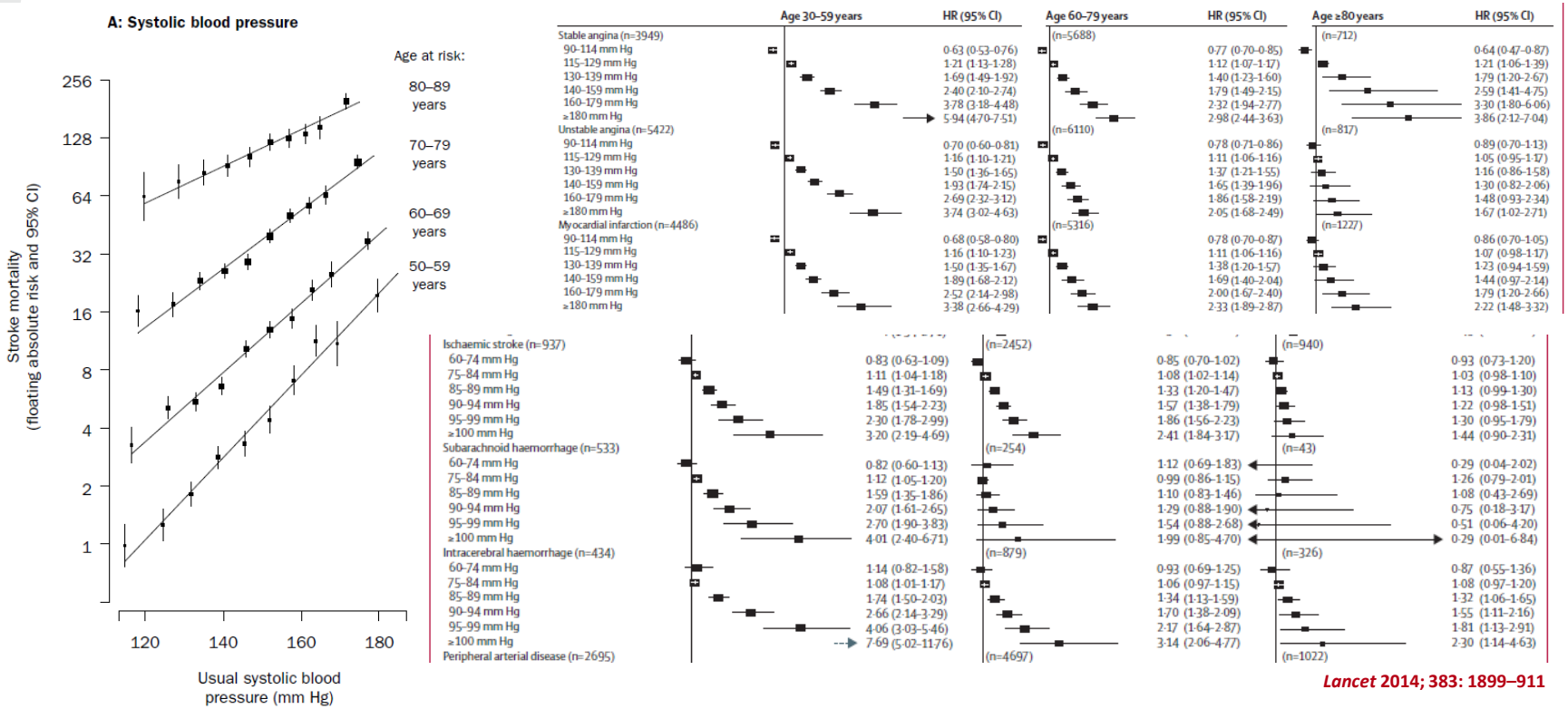
- HTA et dialyse
- HTA et transplantation
- HTA secondaire
- HTA monogénique
- HTA maligne
- Physiopathologie

Plan

- Définition
- Epidémiologie
- Comment on mesure la pression artérielle
- HTA et MRC quel lien?
- Objectif du traitement de l'HTA dans la MRC
- Comment on traite l'HTA dans la MRC
- Des pistes d'avenir.

Définition

- La pression artérielle **associée** au risque cardiovasculaire le plus faible, optimale?, est de **115/75** mm d'Hg. *Lancet* 2002; 360: 1903–13



Lancet 2014; 383: 1899–911

Définitions

- Beaucoup de définitions de l'HTA
  - Indissociable de l'épidémiologie et des essais cliniques
  - Qui produit la définition
  - Comment on mesure la pression artérielle

Table 3 Classification of office blood pressure[a] and definitions of hypertension grade[b]

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension[b]	≥140	and	<90

BP = blood pressure; SBP = systolic blood pressure.
[a]BP category is defined according to seated clinic BP and by the highest level of BP, whether systolic or diastolic.
[b]Isolated systolic hypertension is graded 1, 2, or 3 according to SBP values in the ranges indicated.
The same classification is used for all ages from 16 years.

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European Heart Journal (2018) **39**, 3021–3104
doi:10.1093/eurheartj/ehy339

Table 6. Categories of BP in Adults*

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120–129 mm Hg	and	<80 mm Hg
Hypertension			
Stage 1	130–139 mm Hg	or	80–89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

Hypertension June 2018

Table 1 | **Definitions of hypertension based on the 2013 ESH/ESC guidelines**

Category	Subtype	Systolic BP (mmHg)	Diastolic BP (mmHg)
Office BP	NA	≥140	≥90
Ambulatory BP	Daytime (awake)	≥135	≥85
	Night-time (asleep)	≥120	≥70
	24 h	≥130	≥80
Home BP	NA	≥135	≥85

Définitions

- Un peu d'histoire

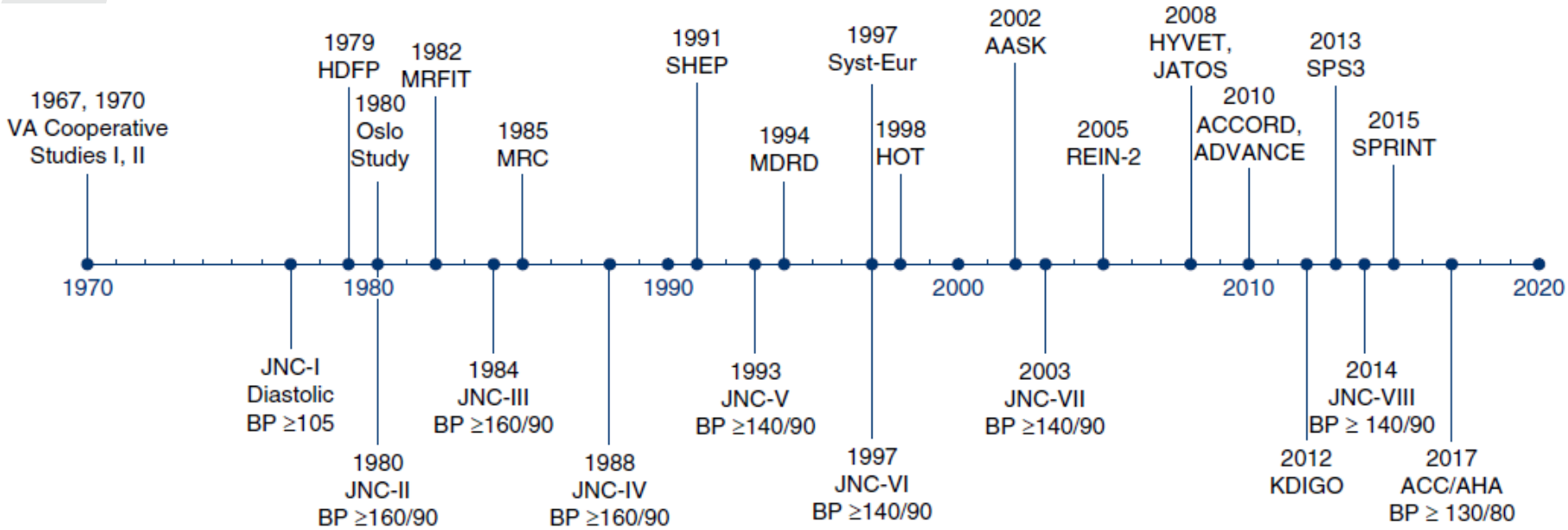


Figure 1. | The Definition of Hypertension per United States BP Guidelines has Changed Over Time. Above timeline: major hypertension trials

Impact des définitions

	SBP/DBP ≥130/80 mm Hg or Self-Reported Antihypertensive Medication†		SBP/DBP ≥140/90 mm Hg or Self-Reported Antihypertensive Medication‡	
Overall, crude	46%		32%	
	Men (n=4717)	Women (n=4906)	Men (n=4717)	Women (n=4906)
Overall, age-sex adjusted	48%	43%	31%	32%
Age group, y				
20–44	30%	19%	11%	10%
45–54	50%	44%	33%	27%
55–64	70%	63%	53%	52%
65–74	77%	75%	64%	63%
75+	79%	85%	71%	78%
Race-ethnicity§				
Non-Hispanic white	47%	41%	31%	30%
Non-Hispanic black	59%	56%	42%	46%
Non-Hispanic Asian	45%	36%	29%	27%
Hispanic	44%	42%	27%	32%

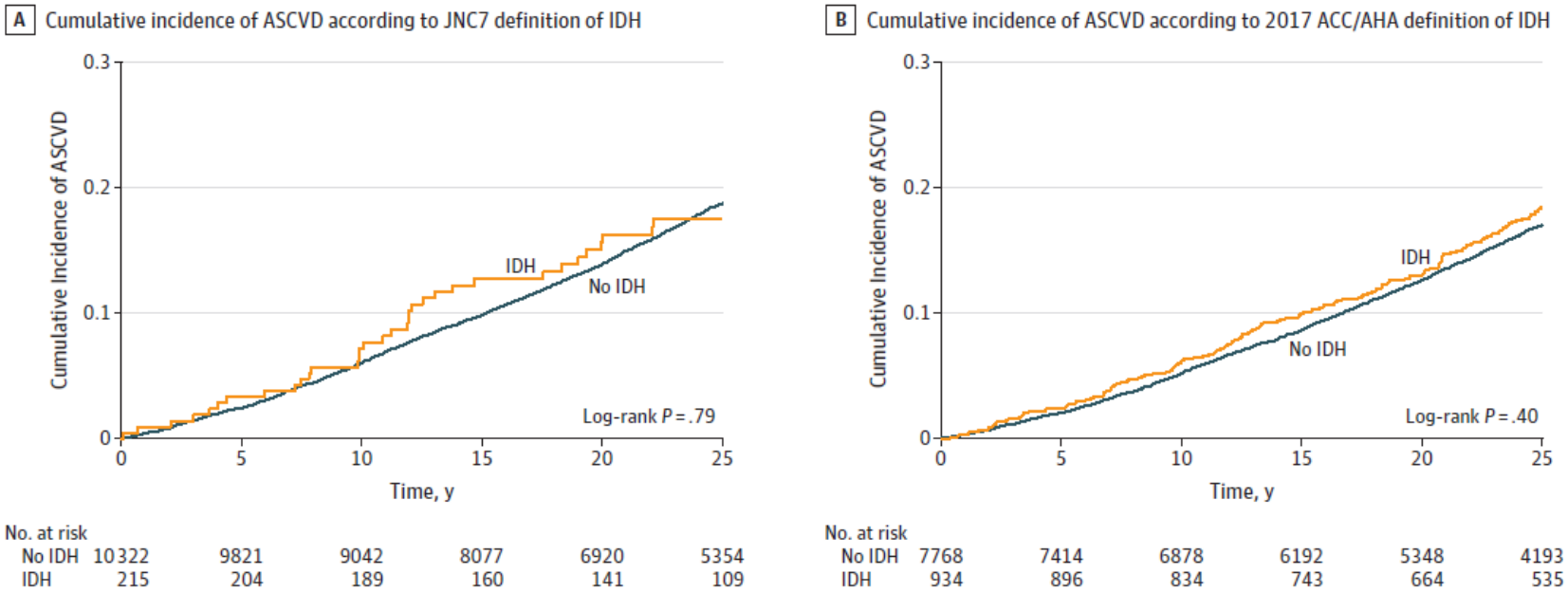
The prevalence estimates have been rounded to the nearest full percentage.

*130/80 and 140/90 mm Hg in 9623 participants (≥20 years of age) in NHANES 2011–2014.

Définitions

- HTA diastolique isolée: aucun effet sur risque CV

Figure 1. Cumulative Incidence of Cardiovascular Events in the Atherosclerosis Risk in Communities (ARIC) Study, According to Both 2003 Joint National Committee (JNC7) and 2017 American College of Cardiology (ACC)/American Heart Association (AHA) Definitions of Isolated Diastolic Hypertension (IDH)



A, The median follow-up in the sample testing the JNC7 definition was 25.1 years (interquartile range [IQR], 16.6-26.4) in the no IDH group and 25.1 years (IQR, 14.6-26.4) in the IDH group. B, The median follow-up in the sample testing the 2017 ACC/AHA definition was 25.2 years (IQR, 17.4-26.5) in the no IDH group and 25.4 years (IQR, 17.9-26.6) in the IDH group. ASCVD indicates atherosclerotic cardiovascular disease.

JAMA. 2020;323(4):329-338.

Définition

- Pour résumer
- La valeur de 140/90 semble une valeur raisonnable à retenir pour parler d'HTA et intervenir sur le plan médicamenteux.
- La valeur de 130/80 doit être retenu comme une alerte pour motiver la mise en place de mesure hygiéno-diététique
- La diastolique isolée semble avoir peut d'intérêt pour porter le diagnostic d'HTA

Définition

- C'est un **facteur de risque cardiovasculaire**.
- Nécessité d'une prise en charge avec l'ensemble des autres facteurs de risque.
- Le traitement de l'HTA, en dehors de l'urgence hypertensive (180/120 et atteinte d'organe), **n'est pas** une urgence thérapeutique.
- Nécessité de bien choisir les modalités thérapeutiques.

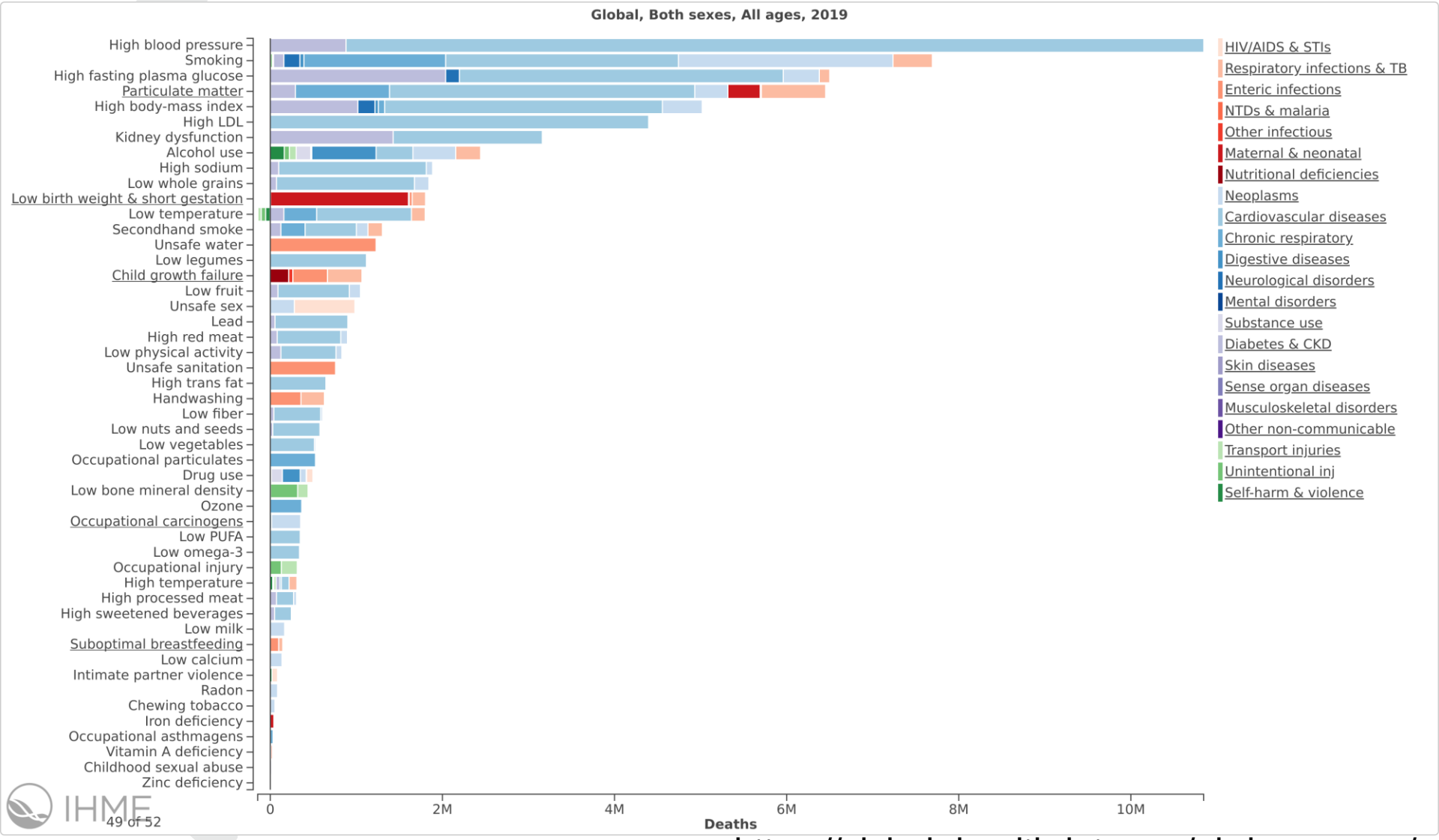
Epidémiologie

- 30% de la population française est hypertendue
- Augmente avec l'âge
- Presqu'un milliard d'individus sont hypertendus dans le monde.
- C'est un vrai problème de santé publique
- C'est **uniquement** un facteur de risque cardiovasculaire.

Epidémiologie

- Entre 40 et 69 ans une augmentation de 20 mm Hg de la TAS ou de 10 mm Hg de la TAD
  - Doublement du risque de mortalité par AVC ou coronaropathie
- Entre 40 et 69 ans une diminution de 5 mm Hg de la TAS :
  - Diminution de 14% de la mortalité par AVC
  - Diminution de 9% de la mortalité par Coronaropathie
- C'est le facteur de risque avec le plus fort impact sur la mortalité dans le monde

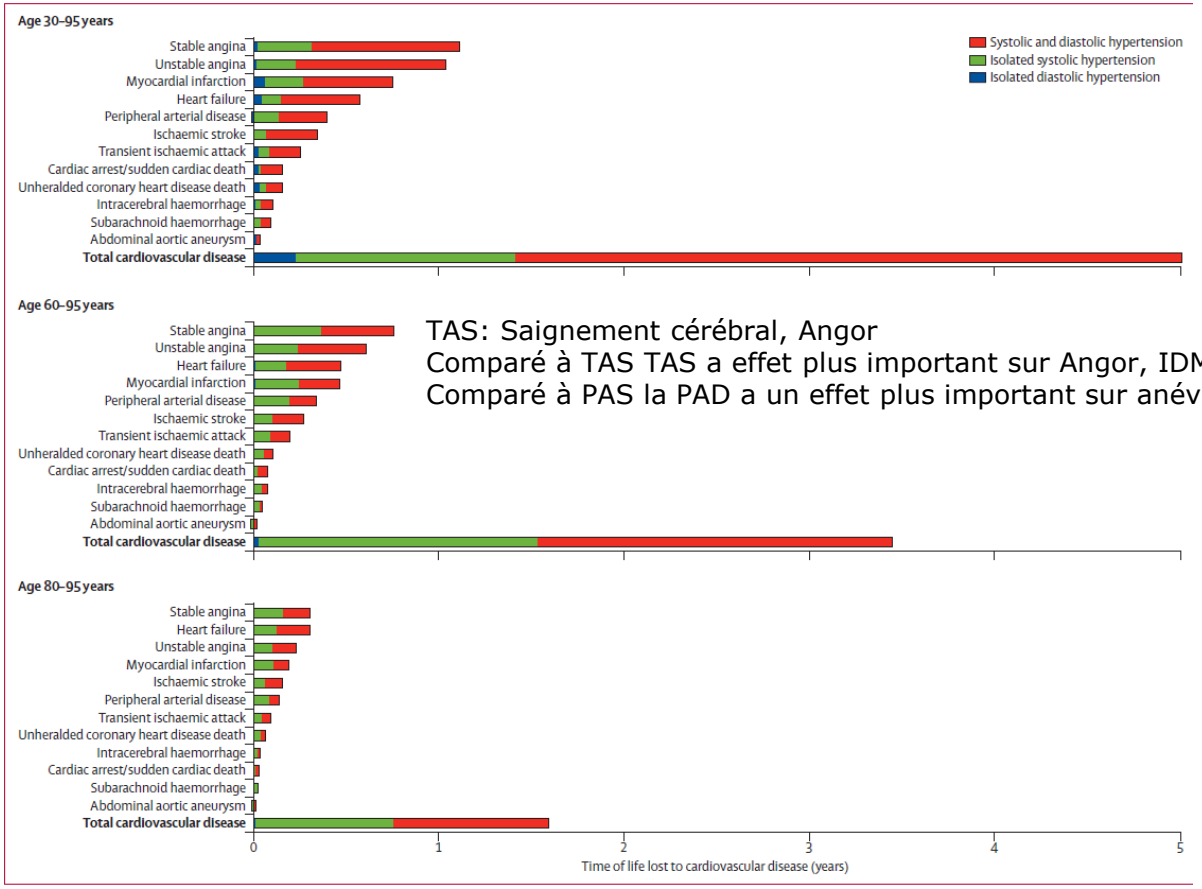
Epidémiologie



https://vizhub.healthdata.org/gbd-compare/

Epidémiologie

- Effet différent de la tension artérielle systolique et diastolique sur le risque cardiovasculaire



TAS: Saignement cérébral, Angor
Comparé à TAS TAS a effet plus important sur Angor, IDM et Artériopathie
Comparé à PAS la PAD a un effet plus important sur anévrysme aorte

Lancet 2014; 383: 1899–911

Epidémiologie

- Pourquoi s'intéresser à l'HTA dans la maladie rénale chronique
  - Une complication fréquente: stade 3 à 4 en France c'est 90% des patients MRC sont hypertendus
  - En pratique le patient avec un DFG à moins de 60 ml/mn/1,73m2 qui n'est pas hypertendu est l'exception.
  - Moins de 50% des patients en stade 3 ou 4 ont une tension artérielle bien contrôlée
- Un problème fréquent et nous sommes mauvais.

Epidémiologie

- La première cause de mortalité au cours de la MRC dans les pays occidentaux est la maladie cardiovasculaire et surtout les coronaires…

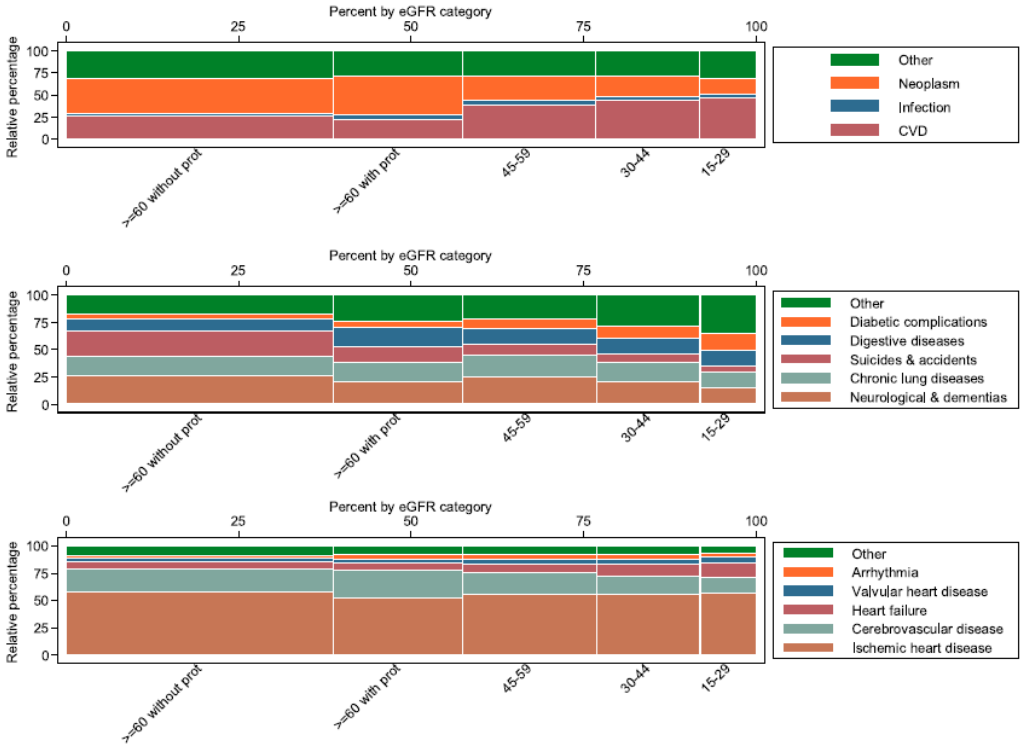
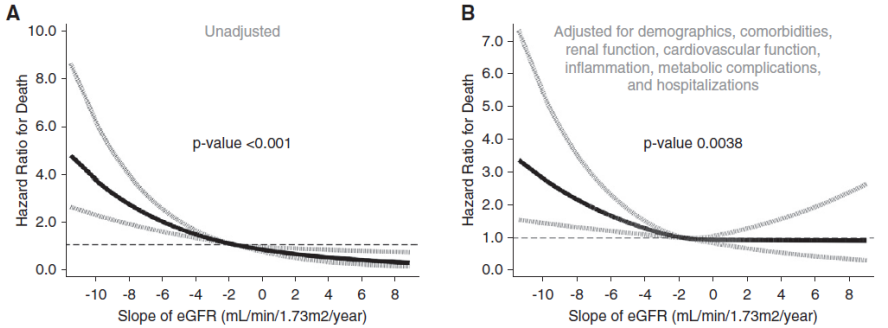


Figure 2. Unadjusted relative percentages for death by cause and eGFR. Top panel shows the relative percentages for death by eGFR

J Am Soc Nephrol 26: 2504–2511, 2015. doi: 10.1681/ASN.2014070714

Epidémiologie

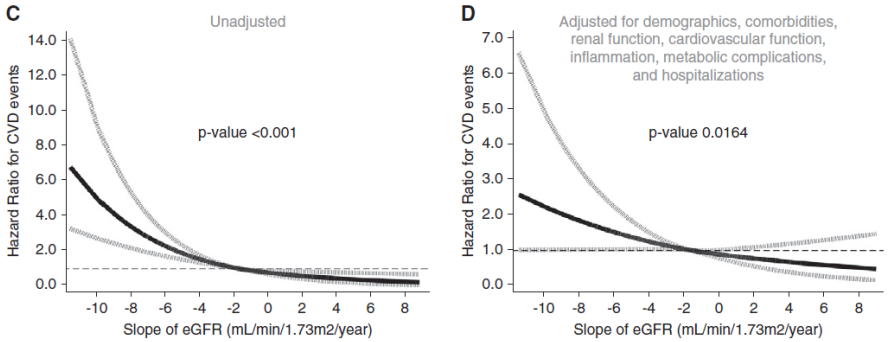
- La pente du DFG est importante sur le risque CV



Décès

Unadjusted hazard ratio (95%CI) for selected values of slopes of eGFR					
Slope	-5.5	-3.5	-1.5	0.5	2.5
HR	1.86	1.36	ref	0.76	0.58
95%CI	1.50 - 2.31	1.24 - 1.48	_	0.65 - 0.88	0.41 - 0.82

Adjusted hazard ratio (95%CI) for selected values of slopes of eGFR					
Slope	-5.5	-3.5	-1.5	0.5	2.5
HR	1.60	1.23	ref	0.95	0.94
95%CI	1.20 - 2.13	1.09 - 1.39	_	0.81 - 1.11	0.65 - 1.35



Evénements CV

Unadjusted hazard ratio (95%CI) for selected values of slopes of eGFR					
Slope	-5.5	-3.5	-1.5	0.5	2.5
HR	2.14	1.45	ref	0.74	0.56
95%CI	1.65 - 2.79	1.30 - 1.62	_	0.63 - 0.87	0.38 - 0.82

Adjusted hazard ratio (95%CI) for selected values of slopes of eGFR					
Slope	-5.5	-3.5	-1.5	0.5	2.5
HR	1.44	1.19	ref	0.86	0.75
95%CI	1.02 - 2.03	1.03 - 1.38	_	0.73 - 1.02	0.51 - 1.11

igure 2. Association between slopes of eGFR and the relative risks of death and CVD events. *JASN* 31: 2912–2923, 2020. doi: https://doi.org/10.1681/ASN.2020040476

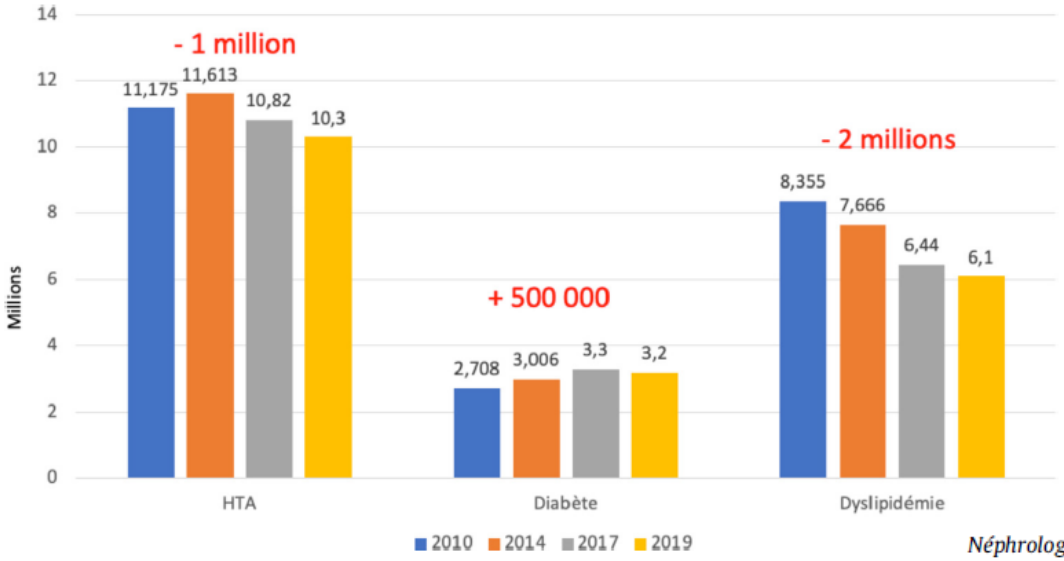
Epidémiologie

- Nous sommes mauvais

Tableau 1
Épidémiologie de l'HTA en France et dans le monde.

Pays	Prévalence HTA	Patients traités, %	Patients contrôles, %	Années	Références
France	31	47	24	2014–2016	[14]
MRC stades 4–5 : en France	91	93	43	2018	[6]
Angleterre	30	58	37	2011	[16]
Allemagne	32	59	51	2008–2011	[15]
USA	34	61	52	2011–2012	[17]
Pays développés	29	56	28	2010	[4]
Pays en développements	32	29	7,7	2010	[4]

HTA : hypertension artérielle ; REF : référence.



Néphrologie & Thérapeutique 16 (2020) 347–352

Epidémiologie

- Pour résumer
- L'HTA est le facteur de risque avec le plus d'impact sur la survie mondiale
- L'HTA est le facteur de risque le plus fréquent
- L'HTA est un facteur de risque cardiovasculaire majeur
- L'HTA est très fréquente dans la maladie rénale chronique
- La maladie cardiovasculaire est la première cause de mortalité des patients MRC
- Nous prenons mal en charge l'HTA

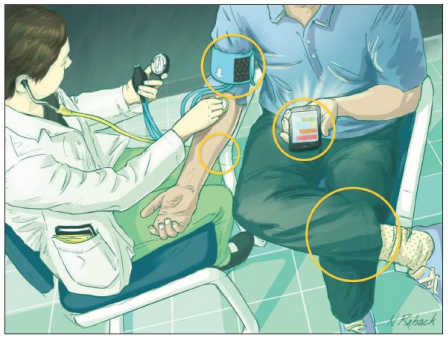
Comment prendre la pression artérielle?

- C'est capital
- Des différences de plusieurs dizaines de mm de Hg sont possibles
- Il s'agit **d'un rituel**
- Il est difficile de bien prendre la tension artérielle en consultation
- La prise à domicile peut être une alternative intéressante
- La mesure ambulatoire n'a pas formellement démontrée une supériorité

Comment prendre la pression artérielle

Etape 1 : Installer correctement le patient

1) Le patient est détendu assis sur une chaise avec les pieds au sol et le dos supporté pendant plus de 5 minutes
2) Pas de prise de caféine, pas de tabac et pas d'exercice physique dans les 30 minutes avant la mesure
3) La vessie doit être vide
4) Ni le patient, ni la personne prenant la mesure ne doivent parler durant la période de repos et la mesure
5) Enlever tous les vêtements recouvrant la zone de mesure
6) Pas de mesure chez un patient assis ou allongé sur une table d'examen.



Comment prendre la pression artérielle

Etape 2 : La technique de mesure

1) Utiliser un appareil de mesure validé et calibré régulièrement
2) Le bras est posé sur un support
3) Le milieu du brassard au bras doit être au niveau de l'atrium droit c.a.d. au milieu du sternum
4) Utilisez la bonne taille de brassard (80% du bras recouvert par la zone gonflée)
5) On utilise aussi bien le diaphragme que la cloche du stéthoscope

Etape 3 : Prendre la bonne mesure

1) A la première visite prendre la pression aux deux bras et garder la mesure la plus haute et ensuite toujours prendre la pression artérielle du même coté
2) Séparer les mesures par 1 à 2 minutes
3) Pour une mesure auscultatoire, déterminer la mesure d'occlusion avec le pouls et gonfler le brassard à 20 ou 30 mm Hg au-dessus de la valeur d'occlusion
4) Dégonfler le brassard de 2mm Hg par seconde

Comment prendre la pression artérielle

Etape 4 : Documenter la mesure

1) Notez la pression artérielle systolique (PAS) et diastolique (PAD).
2) Notez l'heure de la prise la plus proche d'un médicament antihypertenseur

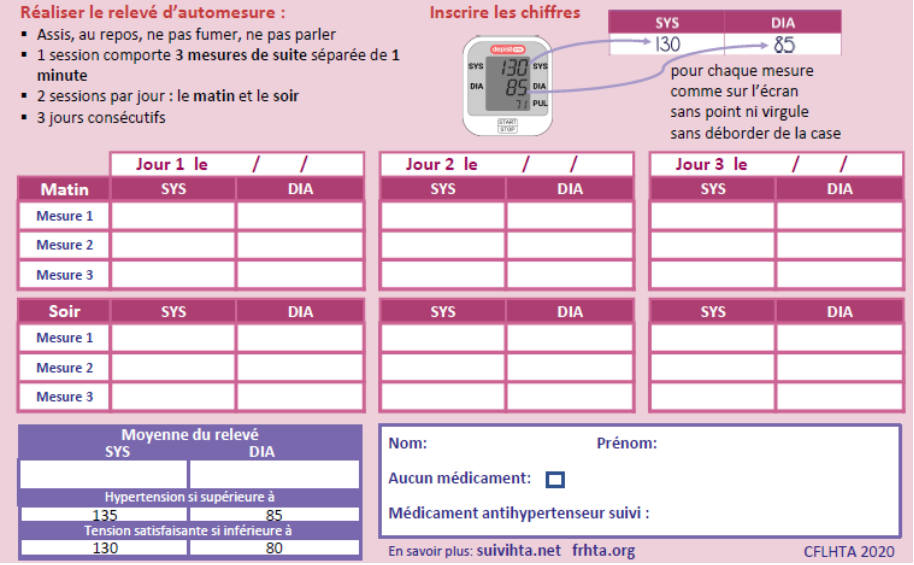
Etape 5 : Faire la moyenne des mesures

- Utilisez la moyenne d'au moins 2 mesures à au moins deux moments différents pour estimer le niveau de pression artérielle.

Etape 6 : Donnez les résultats de la PAS et PAD au patient à l'écrit et à l'oral

Comment prendre la pression artérielle

- A domicile: règle des trois
  - **3 mesures le matin** 20 minutes après le lever et **3 mesures le soir** avant le coucher à réaliser **3 jours de suite**.
  - C'est la moyenne des 18 mesures qui définit un bon contrôle de la tension si elle est inférieure à 135/85.



Réaliser le relevé d'automesure :

- Assis, au repos, ne pas fumer, ne pas parler
- 1 session comporte **3 mesures de suite** séparée de **1 minute**
- 2 sessions par jour : le **matin** et le **soir**
- 3 jours consécutifs

Inscrire les chiffres

SYS	DIA
130	85

pour chaque mesure
comme sur l'écran
sans point ni virgule
sans déborder de la case

	Jour 1 le / /		Jour 2 le / /		Jour 3 le / /	
Matin	**SYS**	**DIA**	**SYS**	**DIA**	**SYS**	**DIA**
Mesure 1						
Mesure 2						
Mesure 3						
Soir	**SYS**	**DIA**	**SYS**	**DIA**	**SYS**	**DIA**
Mesure 1						
Mesure 2						
Mesure 3						

Moyenne du relevé	
SYS	DIA
Hypertension si supérieure à	
135	85
Tension satisfaisante si inférieure à	
130	80

Nom: Prénom:

Aucun médicament: ☐

Médicament antihypertenseur suivi :

En savoir plus: suivihta.net frhta.org

CFLHTA 2020

Comment prendre la pression artérielle

Comparaison mesure clinique et auto mesure à domicile

	Clinique	Auto mesure domicile
PAS/PAD (mm Hg)	120/80	120/80
PAS/PAD	130/80	130/80
PAS/PAD	140/90	135/85
PAS/PAD	160/100	145/90

Savons nous prendre la TA

- Etude sur 159 étudiants de 37 écoles de médecine US, note sur 11

TABLE 2 Percentage of participants correctly performing skills to measure blood pressure accurately, and mean performance score

		Medical education		Age, y		Sex		Planned specialty			
	All (n=159)	1st year (n=98)	2nd to 4th year (n=58)	20–25 (n=104)	≥26 (n=53)	Male (n=86)	Female (n=70)	PC (n=42)	EM (n=17)	Surgery (n=22)	Other (n=22)
Rest 5 min in chair prior to measurement, %	6.9	3.1	12.1[a]	5.8	[illegible]	9.3	2.9	7.1	0	18.2	18.2
Legs uncrossed, %	52.2	50.0	55.2	51.0	[illegible]	44.2	62.9[a]	52.4	58.8	45.5	54.5
Feet on floor, %	15.1	9.2	24.1[a]	10.6	[illegible]	15.1	14.3	16.7	29.4	22.7	13.6
Arm supported, %	61.0	57.1	69.[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	64.3	52.9	63.6	72.7
Correct cuff size, %	73.6	71.4	77.6	[illegible]	[illegible]	[illegible]	[illegible]0.0	78.6	58.8	81.8	72.7
Cuff over bare arm, %	83.0	87.8	79.3	[illegible]	[illegible]	[illegible]	84.3	76.2	88.2	90.9	81.8
No talking, %	57.2	53.1	65.5	54.[illegible]	[illegible]	[illegible].8	58.6	54.8	47.1	45.5	90.9[b]
No mobile phone use/reading, %	17.0	13.3	24.1	17.[illegible]	[illegible]	[illegible].6	15.7	16.7	17.6	13.6	18.2
Checked in both arms, %	18.2	10.2	31.0[b]	17[illegible]	[illegible]	[illegible]9	15.7	19	11.8	22.7	27.3
Noted arm with higher reading, %	15.1	9.2	25.9[b]	[illegible]	17.0	[illegible]	12.9	16.7	11.8	22.7	18.2
Correctly answered which arm to be used to measure in future, %	13.2	8.2	22.4[a]	[illegible]	17.0	[illegible]	10.0	7.1	11.8	22.7	22.7
Mean performance score	4.1	3.7	4.9[b]	4.0	4.5	4.2	4.1	4.1	3.9	4.5	4.9

Abbreviations: EM, emergency medicine; PC, primary care.

J Clin Hypertens. 2017;19:614–619.

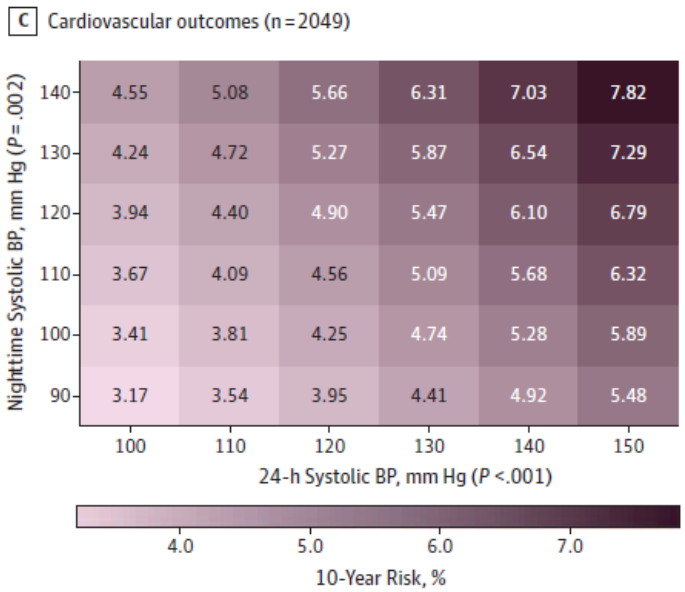
1

Utilité de la MAPA

- 11135 patients (54,7 ans) suivi médian de 13,8 ans. 2836 décès et 2049 événements CV.
- 24h TA et TAS nocturne prédisent mieux mais de façon cliniquement non relevante.

Blood pressure, mm Hg[h]	
Conventional	
Systolic/diastolic, mean	132.4/79.8
SD	23.0/11.8
Automated office	
Systolic/diastolic, mean	135.3/82.3
SD	20.0/11.7
24 hours	
Systolic/diastolic, mean	123.6/73.7
SD	14.3/8.5
Daytime	
Systolic/diastolic, mean	129.7/78.7
SD	15.2/9.2
Nighttime	
Systolic/diastolic, mean	112.6/64.7
SD	15.5/9.4
Dipping ratio[i]	
Systolic/diastolic, mean	0.87/0.83
SD	0.08/0.06

	Adjusted	
Outcomes	Hazard Ratio (95% CI)[c]	*P* Value
Total Mortality (n = 2836)		
Systolic BP index		
Conventional	1.12 (1.08-1.17)	<.001
Automated office systolic BP	1.08 (1.04-1.12)	<.001
Measure times		
24 hours	1.22 (1.16-1.28)	<.001
Daytime	1.14 (1.09-1.20)	<.001
Nighttime	1.23 (1.17-1.28)	<.001
Dipping ratio[d]	1.13 (1.09-1.18)	<.001
All Cardiovascular Outcomes (n = 2049)		
Systolic BP index		
Conventional	1.20 (1.15-1.26)	<.001
Automated office	1.19 (1.14-1.24)	<.001
Measure times		
24 hours	1.45 (1.37-1.54)	<.001
Daytime	1.33 (1.26-1.41)	<.001
Nighttime	1.36 (1.30-1.43)	<.001
Dipping ratio[d]	1.14 (1.08-1.19)	<.001

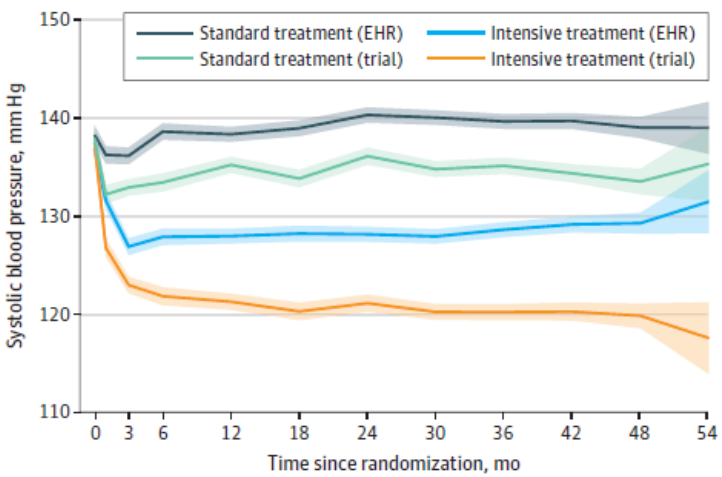


JAMA. 2019;322(5):409-420. doi:10.1001/jama.2019.9811

RCT Vs Real life

- 3074 patients de SPRINT (veterans), comparaison mesure essai et mesure dossiers médicaux. 30% DFG<30 ml/mn/1,73m2.

Figure 2. Systolic Blood Pressure During Follow-up: Trial Measurements vs Outpatient Blood Pressures Extracted From the Electronic Health Record (EHR)



Estimates based on a linear mixed model with random intercepts for participant and clinic sites. Time since randomization was modeled using B-splines. Shaded areas denote 95% pointwise CIs.

Table 2. SBP Trial Measurements vs Outpatient Blood Pressures Extracted From the EHR, by Subgroups

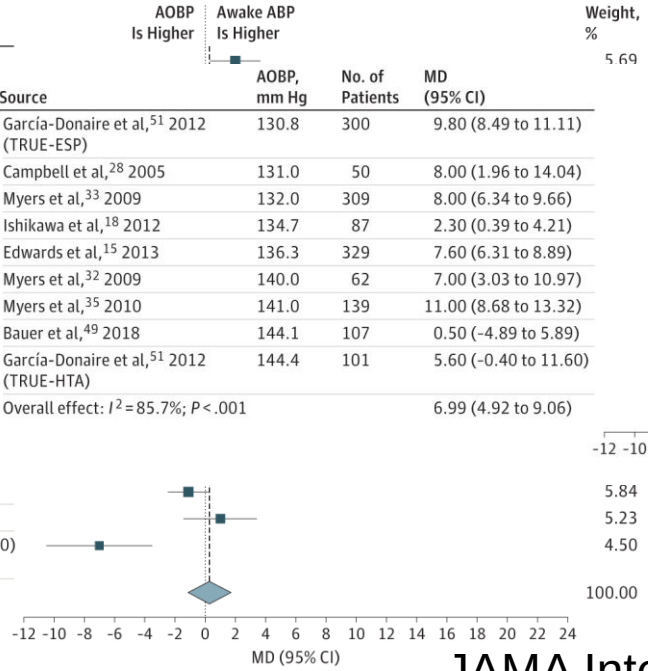
	Intensive treatment				Standard treatment			
	Mean SBP, mm Hg				Mean SBP, mm Hg			
Characteristic	Trial	Outpatient, EHR	Mean difference between trial SBP and EHR SBP (95% CI), mm Hg	*P* value for interaction	Trial	Outpatient, EHR	Mean difference between trial SBP and EHR SBP (95% CI), mm Hg	*P* value for interaction
Overall	120.9	128.2	−7.3 (−7.6 to −7.0)	NA	134.6	139.3	−4.6 (−4.9 to −4.4)	NA
eGFR, mL/min/1.73 m²								
≥60	120.1	127.5	−7.4 (−7.7 to −7.1)	.79	134.5	139.0	−4.5 (−4.8 to −4.2)	.20
<60	122.4	129.6	−7.3 (−7.8 to −6.8)		135.0	139.9	−4.9 (−5.5 to −4.4)	

- Suggère nécessiter d'ajuster de 10 mm Hg la valeur des essais cliniques pour la vraie vie.

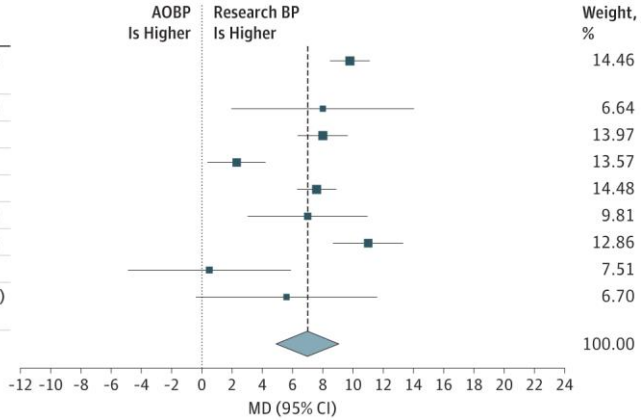
Mesure automatique au cabinet

- En pratique: Omron 907 utilisé dans SPRINT
- Résultat identique à MAPA éveillé

Source	AOBP, mm Hg	No. of Patients	MD (95% CI)
Myers et al,[33] 2009	132.0	309	2.00 (0.33 to 3.67)
Myers,[34] 2010	132.6	254	2.80 (1.15 to 4.45)
Myers et al,[39] 2012	133.1	252	-2.80 (-4.90 to -0.7
Ringrose et al,[41] 2018	133.3	76	13.10 (9.86 to 16.34
Ishikawa et al,[18] 2012	134.7	87	2.40 (-0.63 to 5.43
Myers et al,[38] 2011	135.6	299	-2.30 (-4.29 to -0.31
Padwal et al,[16] 2015	135.7	100	-0.20 (-2.57 to 2.17
Moore et al,[14] 2018	136.0	189	0.00 (-2.21 to 2.21
Edwards et al,[15] 2013	136.3	329	-3.20 (-5.06 to -1.34
Myers et al,[40] 2012	138.6	100	-1.80 (-3.36 to -0.24
Myers et al,[30] 2008 (1 min)	139.0	104	5.00 (1.56 to 8.44)
Godwin et al,[36] 2011	139.2	654	1.70 (0.57 to 2.83)
Andreadis et al,[47] 2012	139.9	139	-5.00 (-7.11 to -2.89
Beckett et al,[27] 2005	140.0	481	1.50 (0.17 to 2.83)
Myers et al,[30] 2008 (2 min)	140.0	100	0.00 (-3.01 to 3.01
Myers et al,[32] 2009	140.0	62	1.00 (-3.27 to 5.27
Armstrong et al,[10] 2015	140.5	422	-1.10 (-2.47 to 0.27)
Myers et al,[35] 2010	141.0	139	1.00 (-1.43 to 3.43)
García-Donaire et al,[51] 2012 (TRUE-HTA)	144.4	101	-7.00 (-10.50 to -3.50)
Overall effect: $I^2 = 89.5\%$; $P < .001$			0.29 (-1.13 to 1.71)



Source	AOBP, mm Hg	No. of Patients	MD (95% CI)
García-Donaire et al,[51] 2012 (TRUE-ESP)	130.8	300	9.80 (8.49 to 11.11)
Campbell et al,[28] 2005	131.0	50	8.00 (1.96 to 14.04)
Myers et al,[33] 2009	132.0	309	8.00 (6.34 to 9.66)
Ishikawa et al,[18] 2012	134.7	87	2.30 (0.39 to 4.21)
Edwards et al,[15] 2013	136.3	329	7.60 (6.31 to 8.89)
Myers et al,[32] 2009	140.0	62	7.00 (3.03 to 10.97)
Myers et al,[35] 2010	141.0	139	11.00 (8.68 to 13.32)
Bauer et al,[49] 2018	144.1	107	0.50 (-4.89 to 5.89)
García-Donaire et al,[51] 2012 (TRUE-HTA)	144.4	101	5.60 (-0.40 to 11.60)
Overall effect: $I^2 = 85.7\%$; $P < .001$			6.99 (4.92 to 9.06)



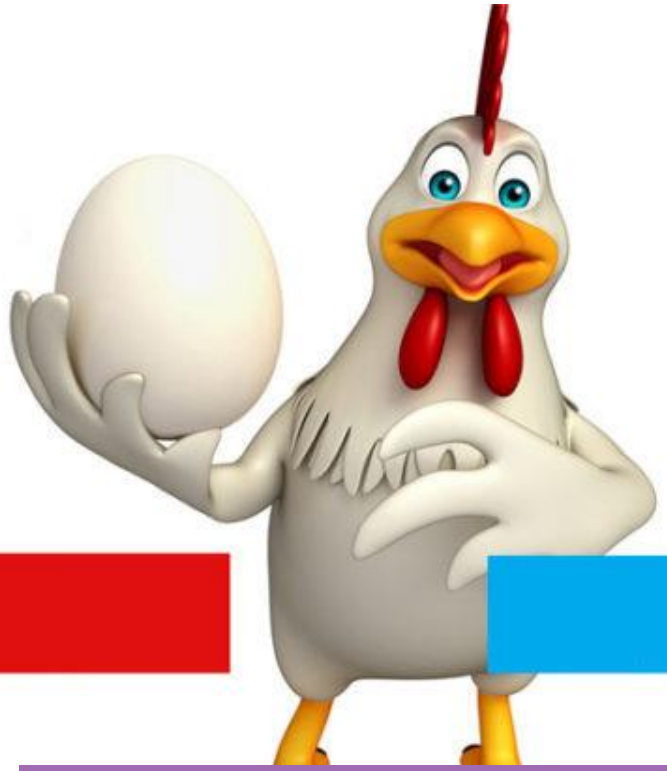
JAMA Intern Med. 2019;179(3):351-362

- Une excellente alternative en clinique

Mesure de la pression artérielle

- En résumé
- Il faut ritualiser et savoir la prendre
- Importance de la méthode pour analyser la valeur
- Intérêt de l'automesure à domicile si bien faite
- MAPA utile pour l'effet blouse blanche
- En cabinet la mesure automatisée est probablement l'avenir.

HTA et MRC: l'œuf ou la poule



Vote MRC

Vote HTA

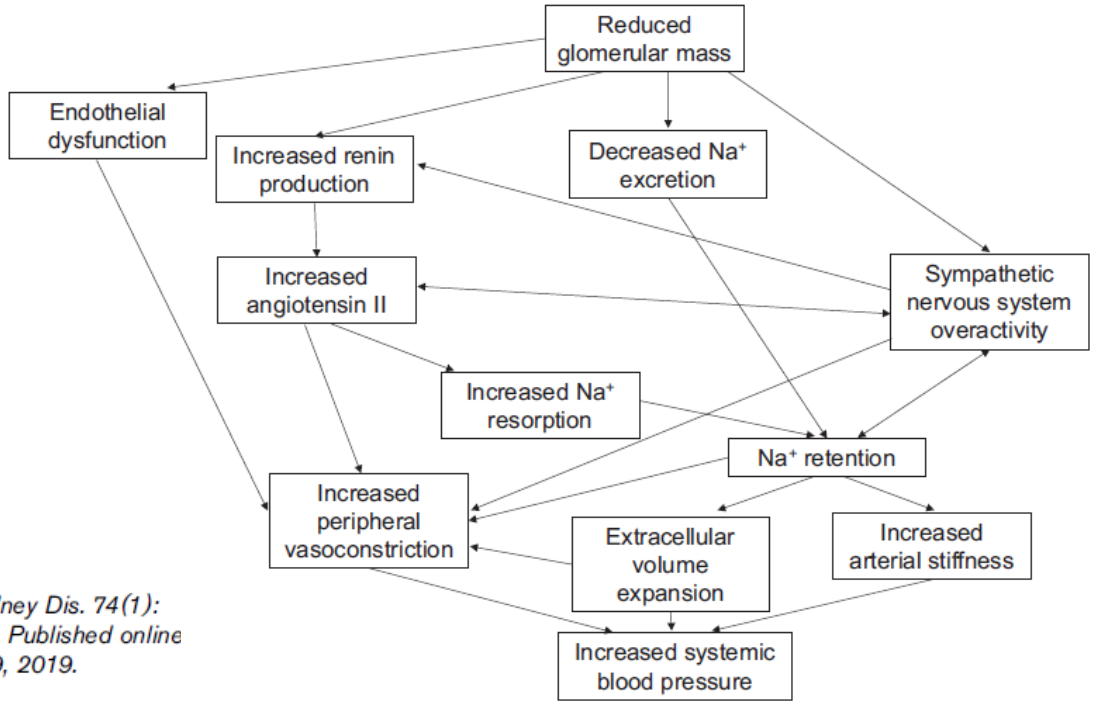
Vote MRC et HTA

HTA et MRC, quel lien?

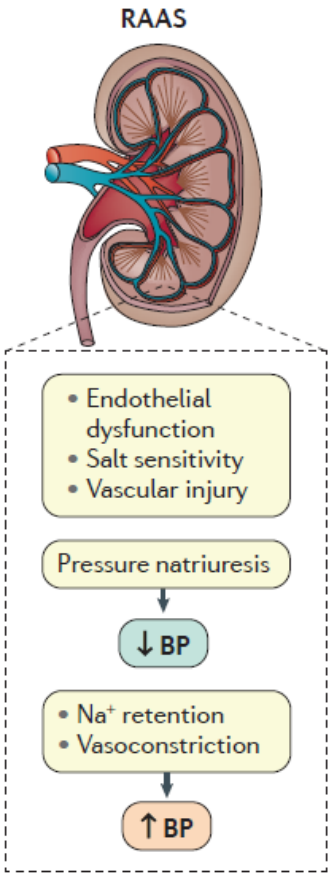
- Est-ce que la MRC est responsable de l'hypertension artérielle?
- Est-ce qu'une hypertension artérielle peut être responsable d'une maladie rénale chronique?
- Est-ce que le contrôle de l'hypertension artérielle est important dans la MRC et pourquoi?

Est-ce que la MRC est responsable de l'hypertension artérielle?

- La réponse est oui sans aucun doute.
  - Argument épidémiologique: 90% des patients en stade 3 ou 5 sont hypertendus
  - Argument physiopathologique



Am J Kidney Dis. 74(1): 120-131. Published online March 19, 2019.



Est-ce que la MRC est responsable de l'hypertension artérielle?

- Argument physiopathologique

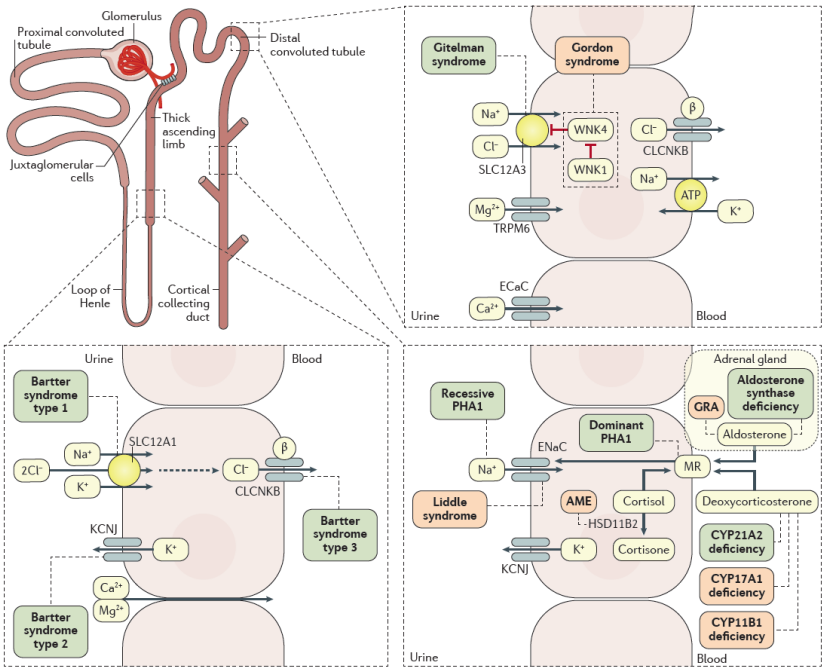


Figure 4 | **Pathways affected in single gene, Mendelian hypertension** GRA, glucocorticoid-remediable aldosteronism; HSD11B2, corticosteroid

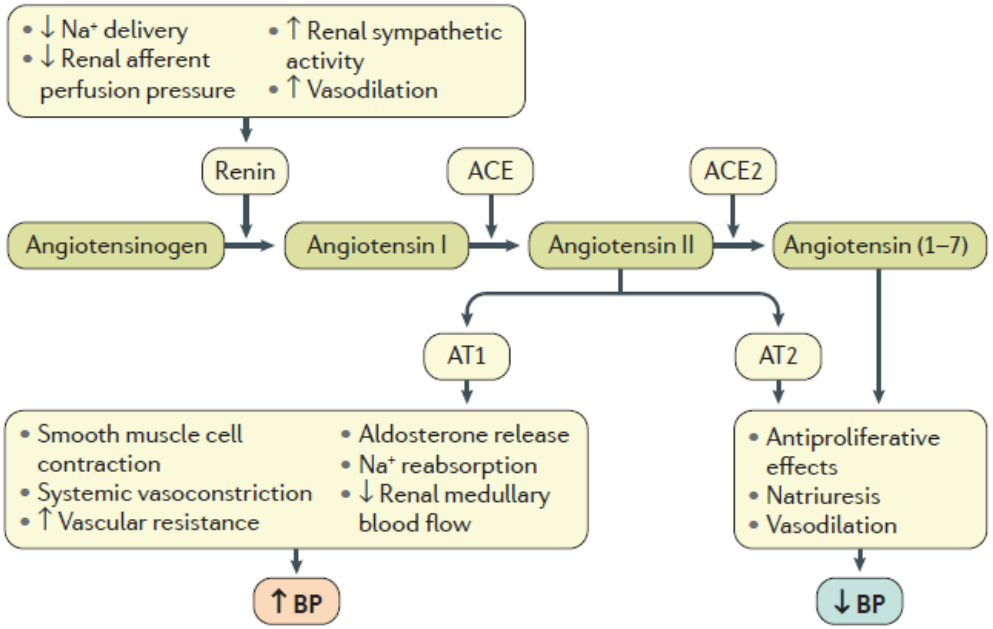


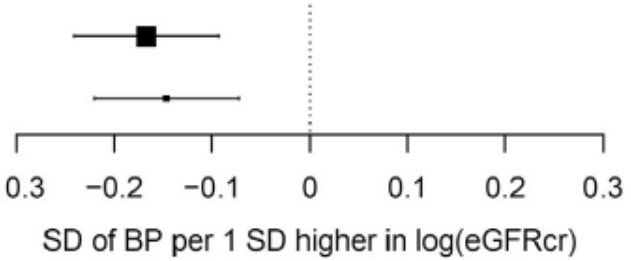
Figure 3 | **Role of the renin–angiotensin–aldosterone system in the regulation of blood pressure.** Decreased renal afferent arteriolar perfusion pressure, reduced sodium

doi:10.1038/nrdp.2018.14

Est-ce que la MRC est responsable de l'hypertension artérielle?

- Un peu de randomisation mendélienne

Exposure	Outcome	No. of SNPs	Effect [95% CI]	*P* value
eGFRcr	SBP	33	−0.17 [−0.24, −0.09]	9.92E−05
	DBP	33	−0.15 [−0.22, −0.17]	5.02E−04



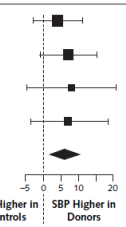
Kidney International (2020) **98,** 708–716;

  - Une diminution de 50% du DFGe est associé à une augmentation de 17,5/8,4 mmHg de la TA

- Un peu de transplantation: TAS: +6 mmHg

Figure 1. Meta-analysis of controlled studies of systolic blood pressure (*SBP*) and diastolic blood pressure (*DBP*) at least 5 years after kidney donation.

Study, Year (Reference)	Donors, after Donation: Mean Years after Donation, (Range)*	Donors, *n*	Mean Value SBP (SD), *mm Hg*†	Use of Antihypertensive Medications, %	Control Participants: Controls, *n*	Mean Value SBP (SD), *mm Hg*†	Use of Antihypertensive Medications, %	Mean Difference in SBP (95% CI), *mm Hg*
Najarian et al., 1992 (50)	8 (1–19)	57	134 (15)	32	50	130 (21)	44	4 (−3.1 to 11.1)
Undurraga et al., 1998 (53)	11 (1–21)	30	125 (18)	NR	30	118 (13)	NR	7 (−0.9 to 15.2)
Talseth et al., 1986 (54)	11 (10–12)	32	140 (23)	10	32	132 (29)	NR	8 (−4.8 to 20.8)
Williams et al., 1986 (57)	13 (10–18)	38	136 (25)	‡	16	129 (16)	‡	7 (−3.7 to 18.5)
Pooled estimate		157	133 (6)		128	126 (8)		6 (1.6 to 10.5)



Ann Intern Med. 2006;145:185-196.

Est-ce que l'HTA est responsable d'une maladie rénale chronique?

- La réponse est difficile et actuellement plutôt non.
- Les urgences hypertensives peuvent s'accompagner d'une IRA qui peuvent faire le lit de la MRC.
- Il n'y a aucun doute sur le fait que des pression artérielle >180/120 puissent s'accompagner du développement d'une MRC.
- Pour des tensions artérielles plus physiologiques quelles sont les preuves?

Est-ce que l'HTA est responsable d'une maladie rénale chronique?

- Epidémiologique
  - Pour: 316000 personnes, DFGe>60 sans Pu, suivi> 8 millions année patients (48567 décès)

Table 2. Age-Adjusted Rates of ESRD and Multivariable Risk of ESRD for Each Category of Blood Pressure*

Blood Pressure Category	No. of Persons	Mean Systolic/ Diastolic Blood Pressure, mm Hg	No. of ESRD Events	Age-Adjusted Rate per 100 000 Person-Years (95% CI)	RR (95% CI) Multivariable Risk†	RR (95% CI) Adjusted Further for Serum Creatinine
Optimal	89 774	109/66	106	4.5 (3.6-5.8)	1.00	1.00
Normal, not optimal	72 192	122/73	182	9.3 (7.5-11.5)	1.61 (1.27-2.05)	1.62 (1.27-2.07)
High normal	56 078	132/77	192	12.9 (10.3-16.0)	1.97 (1.54-2.51)	1.98 (1.55-2.52)
Hypertension						
Stage 1	69 083	143/83	379	19.5 (15.8-24.1)	2.57 (2.06-3.22)	2.59 (2.07-3.25)
Stage 2	21 340	161/92	199	31.7 (24.6-41.0)	3.82 (2.97-4.92)	3.86 (3.00-4.96)
Stage 3	6626	177/101	70	34.5 (24.7-48.0)	3.88 (2.82-5.33)	3.88 (2.82-5.34)
Stage 4	1582	189/122	21	43.7 (26.9-71.1)	4.18 (2.59-6.76)	4.25 (2.63-6.86)
Total	**316 675**		**1149**			

Arch Intern Med. 2005;165:923-928

  - Contre: 1594 personnes, DFG mesuré, suivi 5,6 ans

Table 3 | The associations between baseline blood pressure and GFR change rates in linear mixed regression analyses: RENIS-FU

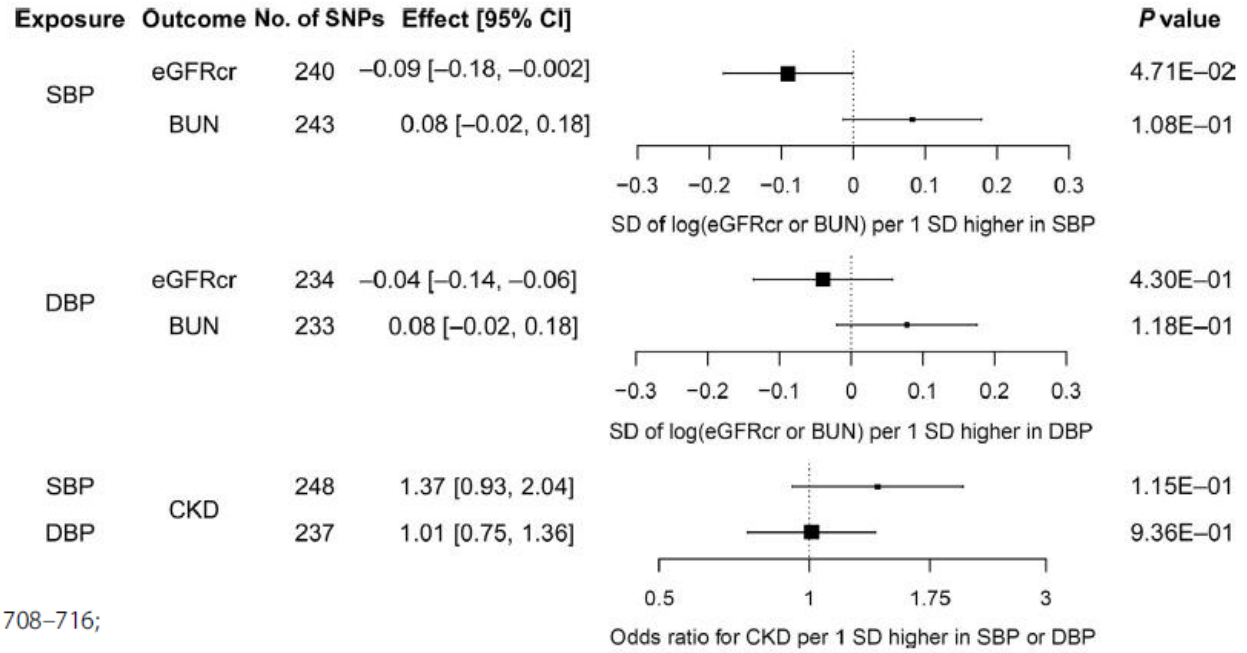
BP component	Model 1[a] β (ml/min/yr)	Model 1[a] 95% confidence interval	Model 1[a] *P* value	Model 2[b] β (ml/min/yr)	Model 2[b] 95% confidence interval	Model 2[b] *P* value
Systolic BP per 10 mm Hg	−0.05	−0.12 to 0.03	0.21	−0.02	−0.09 to 0.06	0.69
Diastolic BP per 10 mm Hg	−0.04	−0.17 to 0.09	0.56	0.02	−0.11 to 0.16	0.72
Pulse pressure per 10 mm Hg	−0.07	−0.18 to 0.03	0.17	−0.05	−0.15 to 0.06	0.41
Mean arterial pressure per 10 mm Hg	−0.05	−0.16 to 0.06	0.34	0.00	−0.12 to 0.12	1.00

Each horizontal section in the table corresponds to 1 linear mixed regression model. Negative coefficients indicate a steeper GFR decline, and positive coefficients indicate a slower decline.
BP, blood pressure; GFR, glomerular filtration rate; RENIS-FU, the Renal Iohexol Clearance Survey Follow-Up Study.

Kidney International (2016) **90,** 404–410;

Est-ce que l'HTA est responsable d'une maladie rénale chronique?

- Un peu de randomisation mendélienne
  - Aucun effet de la pression artérielle sur le risque de maladie rénale chronique



Kidney International (2020) **98,** 708–716;

Figure 3 | Estimates of causal effect of systolic blood pressure (SBP) and diastolic blood pressure (DBP) on log(glomerular filtration rate estimated from serum creatinine [eGFRcr]), log(blood urea nitrogen [BUN]), and chronic kidney disease (CKD) calculated using the weighted mode method. CI, confidence interval.

Est-ce que l'HTA est responsable d'une maladie rénale chronique?

- Un peu d'intervention
  - Est-ce qu'un contrôle stricte de la PA diminue le risque de faillite rénale?

	Trials (n)	Events (n)/patients (n)	Mean blood pressure difference (mm Hg)	Relative risk (95% CI)
Other major vascular events and renal outcomes				
Heart failure	10	189/13 698 *vs* 221/19 608	−7·2/−4·0	0·85 (0·66–1·11)
End-stage kidney disease	8	248/4533 *vs* 266/4157	−9·4/−5·1	0·90 (0·77–1·06)
Albuminuria	3	926/2661 *vs* 988/2563	−10·1/−6·4	0·90 (0·84–0·97)
Retinopathy	4	342/1421 *vs* 351/1244	−11·2/−6·3	0·81 (0·66–1·00)
Mortality				
Cardiovascular death	13	354/18 209 *vs* 446/24 163	−6·9/−3·5	0·91 (0·74–1·11)
Non-cardiovascular death	12	385/18 027 *vs* 476/23 966	−6·9/−3·6	0·98 (0·86–1·13
Overall mortality	**19**	**794/19 537 *vs* 968/25 452**	**−6·8/−3·5**	**0·91 (0·81–1·03)**

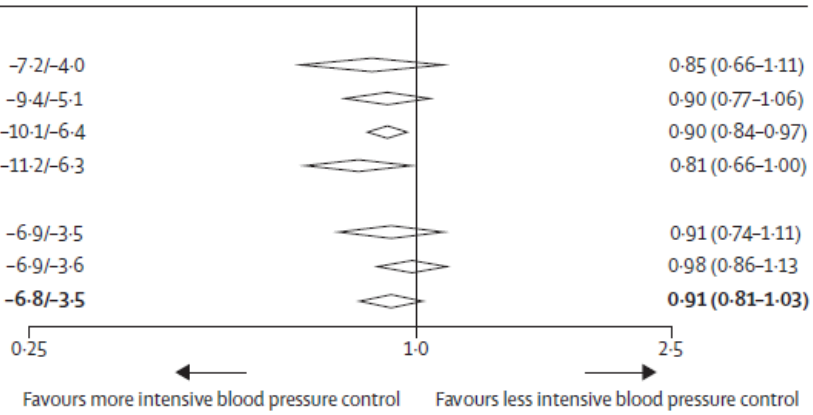


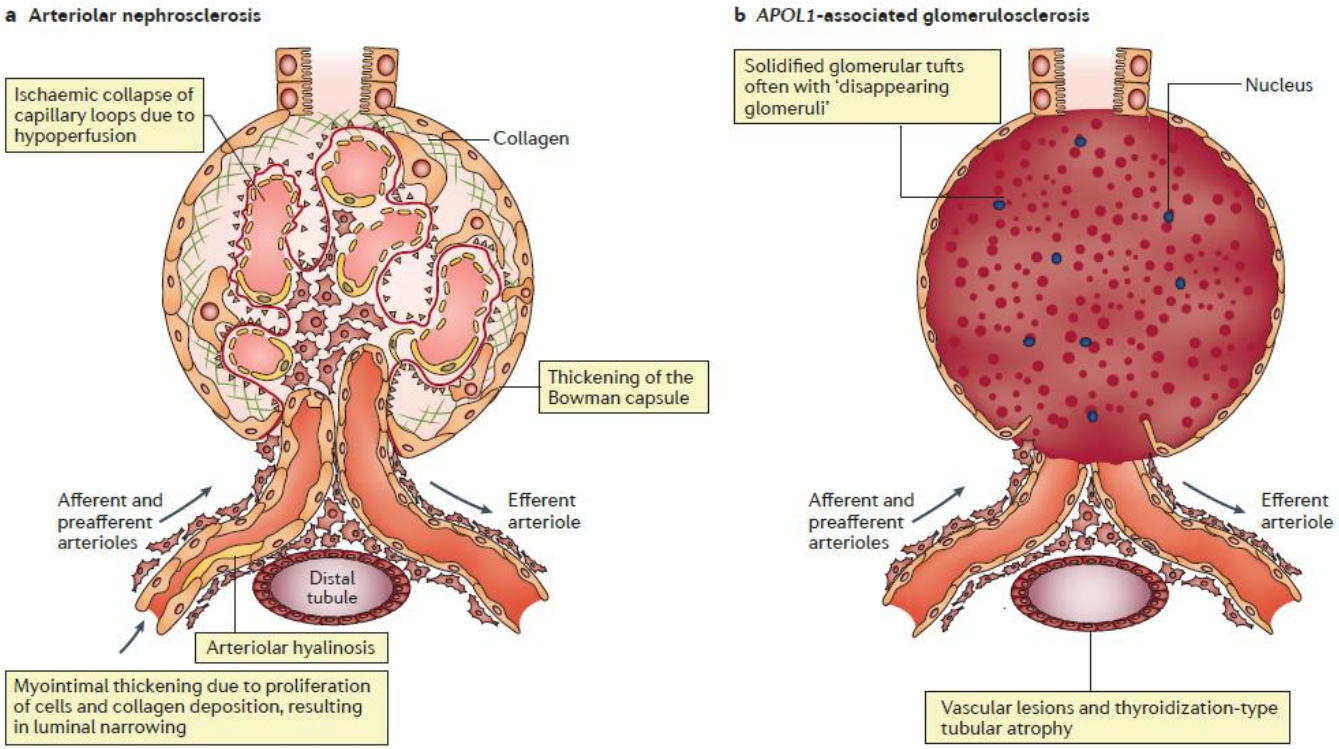
Figure 3: Effect of intensive versus less intensive blood pressure lowering on the risk of other major vascular events, renal outcomes, and mortality

Lancet 2016; 387: 435–43

- Peu d'arguments pour penser que la néphropathie hypertensive existe.

Est-ce que l'HTA est responsable d'une maladie rénale chronique?

- Abandonnons la néphropathie hypertensive pour reconnaitre une maladie rénale vasculaire primitive.



doi:10.1038/nrneph.2015.172
Published online 10 Nov 2015

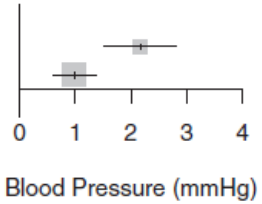
Figure 1 | **Schematic representation of vascular and glomerular lesions in hypertension-attributed nephropathy. a** | Features of arteriolar

Il n'y a pas que le DFG dans la vie

- L'albuminurie augmente le niveau de pression artérielle
- La pression artérielle augmente l'albuminurie

A

Exposure	Outcome	SNPs in score	mmHg Blood Pressure [95%CI] per 1–SD Increase in Albuminuria	P value
Albuminuria	Systolic Blood Pressure	44	2.16 [1.51; 2.82]	1.22e–10
Albuminuria	Diastolic Blood Pressure	44	0.99 [0.61; 1.36]	3.40e–07



B

Exposure	Outcome	SNPs in score	SD Albuminuria [95%CI] per 1–mmHg Increase in Blood Pressure	P value
Systolic Blood Pressure	Albuminuria	47	0.005 [0.004; 0.006]	2.45e–13
Diastolic Blood Pressure	Albuminuria	52	0.007 [0.005; 0.009]	1.83e–09

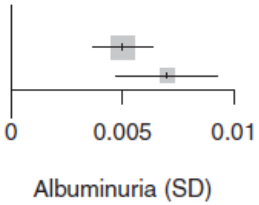


Figure 4. Bidirectional Mendelian Randomization Identifies Suggestive Causal Effects of Albuminuria on Blood Pressure and of Blood Pressure on Albuminuria

American Journal of Human Genetics (2018), https://doi.org/10.1016/j.ajhg.2018.08.004

Est-ce que le contrôle de l'HTA est important dans la MRC et pourquoi?

- L'HTA est un facteur de risque cardiovasculaire, la première cause de mortalité dans la MRC est la maladie cardiovasculaire.
- Quel effet a un contrôle strict de l'HTA?
  - SPRINT-CKD: 2646 patients randomisés, 72 ans, 40% de femmes, DFGe: 48 ml/mn, Albuminurie médiane 13mg/g

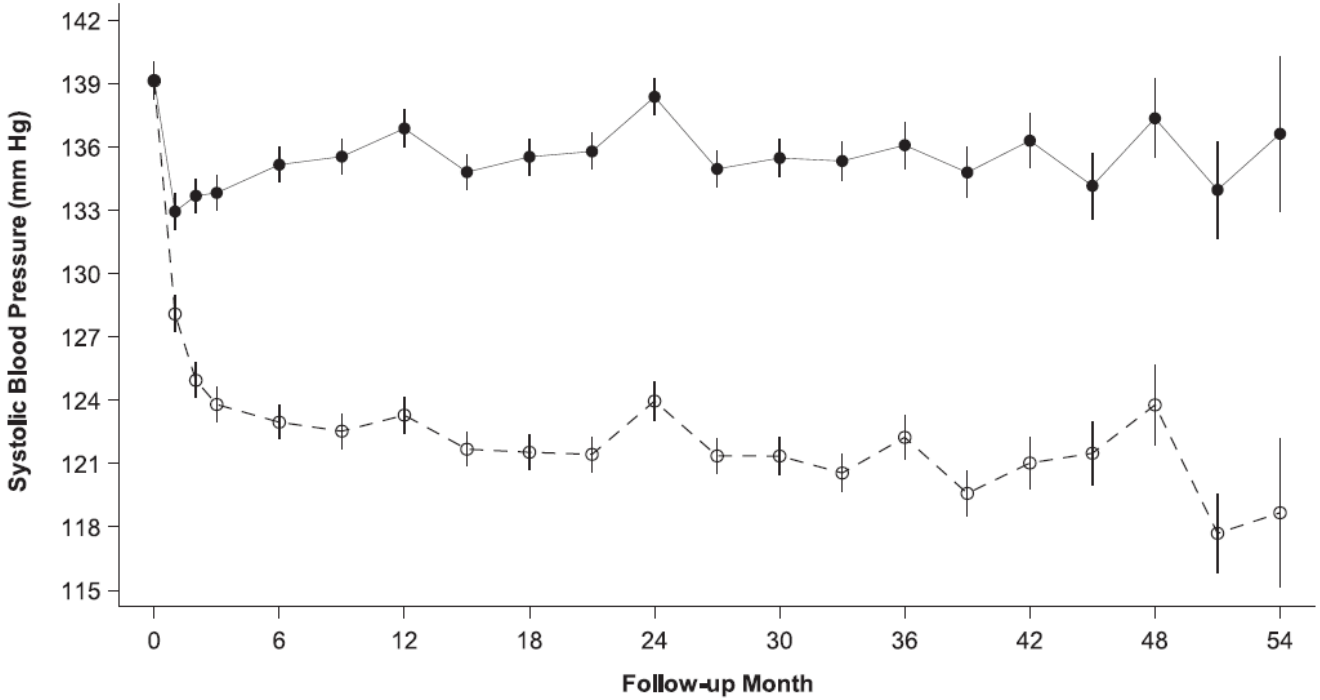
Table 2. Use of antihypertensive medications during follow-up in the SPRINT participants with CKD

Medication Usage	Intensive Treatment, *n*=1330	Standard Treatment, *n*=1316
No. of medications		
Mean no. of medications (SD)	2.90 (1.24)	2.02 (1.23)
Zero medications, no. (%)	25 (1.9)	123 (9.3)
One medication, no. (%)	124 (9.3)	359 (27.3)
Two medications, no. (%)	376 (28.3)	399 (30.3)
Three medications, no. (%)	398 (29.9)	278 (21.1)
Four or more medications, no. (%)	407 (30.6)	157 (11.9)

J Am Soc Nephrol 28: 2812–2823, 2017.

SPRINT-CKD

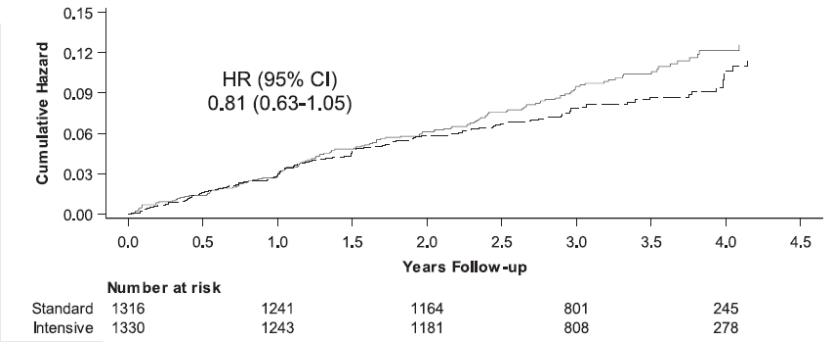
- Baisser la pression sous les 120 mm Hg de systolique c'est possible



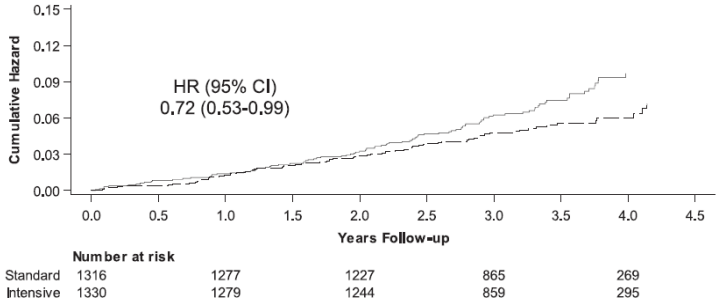
Number With Data										
Standard:	1316	1215	1156	1117	1087	1022	766	480	230	46
Intensive:	1330	1246	1194	1145	1136	1054	804	515	268	58
Mean Number of Meds										
Standard:	2.1	2.0	2.0	2.0	2.1	2.0	2.1	2.1	2.1	2.0
Intensive:	2.1	2.9	3.0	3.0	3.0	3.0	2.9	2.9	3.0	3.1

SPRINT-CKD

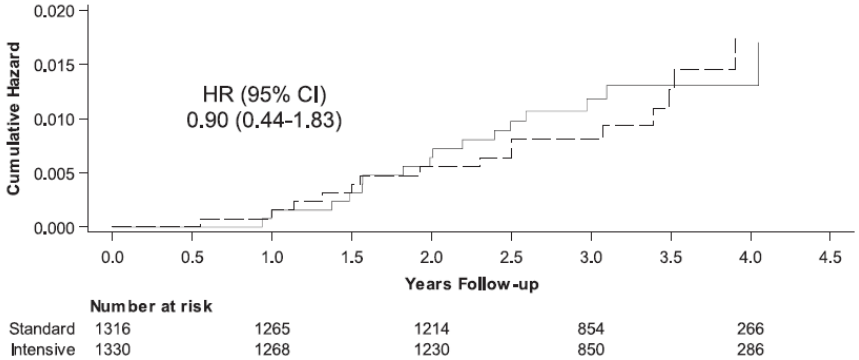
- Ca fait quoi?
  - Critère principal: IDM, SCA, AVC, ICC, Décès CV



  - Mortalité toute cause

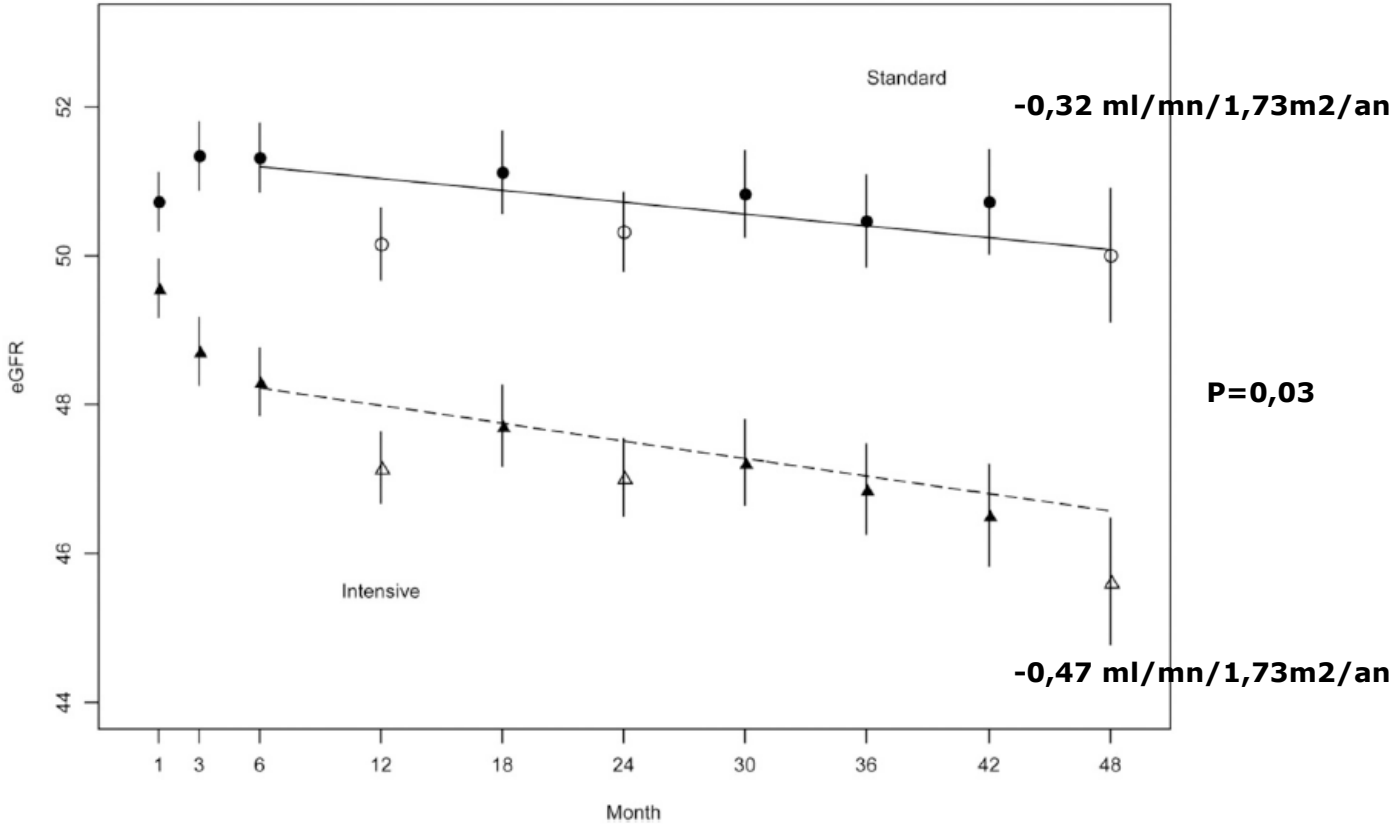


  - Rein: Diminution de >50% DFG ou faillite rénale



SPRINT-CKD

- Et sur la pente de DFG?



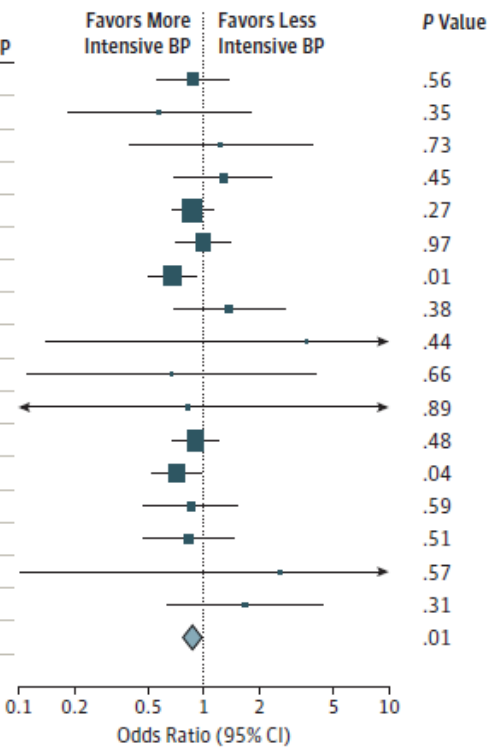
Est-ce que le contrôle de l'HTA est important dans la MRC et pourquoi?

- Et une petite méta-analyse sur la mortalité

Figure 2. Effect of Intensive Blood Pressure (BP) Lowering on Risk of Mortality in Hypertensive Trial Participants With Chronic Kidney Disease

Source	Odds Ratio (95% CI)	Score	No. of Deaths/Total No. More Intensive BP	No. of Deaths/Total No. Less Intensive BP	P Value
Wright et al,[14] 2002	0.874 (0.554-1.380)	-0.578	37/540	43/554	.56
Estacio et al,[24] 2000	0.575 (0.182-1.820)	-0.941	5/62	9/68	.35
Schrier et al,[26] 2002	1.227 (0.398-3.865)	0.349	6/57	7/80	.73
Cushman et al,[32] 2010	1.271 (0.685-2.360)	0.761	26/208	20/198	.45
Heerspink et al,[27] 2010	0.862 (0.662-1.123)	-1.102	117/1010	135/1023	.27
Lonn et al,[37] 2016	0.993 (0.699-1.410)	-0.039	49/1220	97/2399	.97
Beckett et al,[30] 2008	0.676 (0.502-0.911)	-2.570	83/788	121/816	.01
Klahr et al,[13] 1994	1.366 (0.681-2.742)	0.878	20/432	14/408	.38
Mant et al,[34] 2016	3.588 (0.140-91.945)	0.772	1/26	0/30	.44
Ruggenenti et al,[22] 2005	0.667 (0.110-4.042)	-0.441	2/167	3/168	.66
Schrier et al,[25] 2002	0.825 (0.050-13.701)	-0.134	1/41	1/34	.89
SHEP Cooperative Research Group,[28] 1991	0.900 (0.670-1.209)	-0.700	96/879	103/859	.48
Wright et al,[17] 2015	0.714 (0.519-0.982)	-2.072	70/1330	95/1316	.04
Benavente et al,[33] 2013	0.850 (0.468-1.544)	-0.534	24/216	25/195	.59
Staessen et al,[29] 1997	0.826 (0.470-1.451)	-0.665	26/242	29/228	.51
Toto et al,[23] 1995	2.566 (0.101-64.993)	0.572	1/42	0/35	.57
UK Prospective Diabetes Study Group,[35] 1998	1.667 (0.626-4.435)	1.023	20/68	7/35	.31
Overall	0.859 (0.764-0.965)	-2.560	584/7451	709/8473	.01

Heterogeneity: $\tau^2 = 0\%$; $P = .77$; $I^2 = 0\%$



JAMA Intern Med. doi:10.1001/jamainternmed.2017.4377

Est-ce que le contrôle de l'HTA est important dans la MRC et pourquoi?

- Et une petite méta-analyse sur la mortalité (AASK, MDRD, ACCORD, SPRINT)

Table 1. Baseline Characteristics of Study Participants

Characteristic	Intensive Therapy, N=2509	Standard Therapy, N=2474
Age, y	64±13.5	64±13.6
Female sex, n (%)	1039 (41.4)	1024 (41.4)
Race or ethnic group, n (%)		
White	1384 (55.2)	1381 (55.8)
Black	933 (37.2)	922 (37.3)
Hispanic	129 (5.1)	128 (5.2)
Other	63 (2.5)	43 (1.7)
Baseline SBP status, n		
130≤ SBP <140	604	609
SBP ≥140	1197	1171
Laboratory values		
Baseline SBP, mm Hg	140.6±18.6	140.3±19.4
Baseline DBP, mm Hg	80.4±14.6	79.9±14.8
Fasting total cholesterol, mg/dL	198±46.2	197.8±45.3
Fasting glucose, mg/dL	102.1±31.1	101.8±31.9
Body mass index	29.6±5.9	29.5±6.0
Serum creatinine, mg/dL	1.7±0.7	1.7±0.7
Estimated GFR, mL/min per 1.73 m^2	45.4±12.3	45.3±12.1
Smoking status, n (%)		
Current smoker	550 (21.9)	513 (20.7)
Former smoker	803 (32.0)	827 (33.4)
Never smoker	1180 (47.0)	1160 (46.9)

Baseline characteristics for the standard and intensive groups. DBP indicates diastolic blood pressure; and SBP, systolic BP.

Table 2. Primary and Secondary Outcomes

Outcome	Intensive Treatment		Standard Treatment		Hazard Ratio	*P* Value
	Total Events	% Per Year	Total Events	% Per Year		
Primary outcome (N_{total}=4983)	N=2509		N=2474			
All-cause mortality	153	1.71	173	1.95	0.87 (0.69–1.08)	0.211
Primary outcome (after exclusion)* (N_{total}=4564)	N=2299		N=2265			
All-cause mortality (after exclusion)*	130	1.63	162	2.06	0.79 (0.63–1.00)	0.048
Secondary outcomes (N_{total}=4143)	N=2077		N=2066			
CV mortality	45	0.59	53	0.70	0.82 (0.55–1.23)	0.338
CV composite	215	2.92	238	3.28	0.87 (0.72–1.05)	0.151
Secondary outcomes (after exclusion)* (N_{total}=3724)	N=1867		N=1857			
CV composite (after exclusion)*	180	2.79	208	3.30	0.82 (0.67–1.01)	0.060

Primary and secondary outcomes for the intensive and standard groups. ACCORD indicates Action to Control Cardiovascular Risk in Diabetes; and CV, cardiovascular.
*After excluding patients with GFR ≥60 mL/min per 1.73 m^2 and those in the intensive glycemic group of ACCORD.

Hypertension. 2019;73:1275-1282.

125.0/71.1 vs 136.9/77.4 mm Hg

Est-ce que le contrôle de l'HTA est important dans la MRC et pourquoi?

- Sur la fonction rénale, aucun essai n'a montré de bénéfice d'un contrôle strict de la pression artérielle sauf MDRD et AASK dans le sous groupe avec **une protéinurie**.

Clin J Am Soc Nephrol 14: 161–169, 2019. doi: https://doi.org/10.2215/CJN.07440618

- Une petite alerte sur le contrôle strict et le risque de maladie rénale chronique

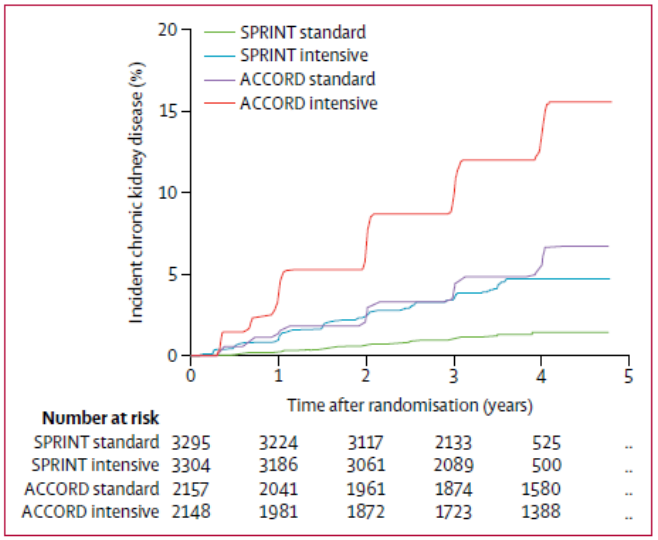
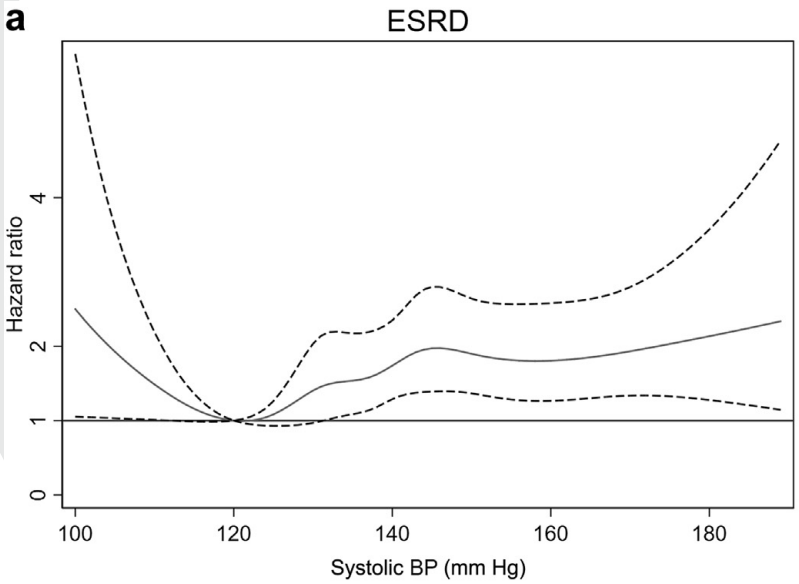
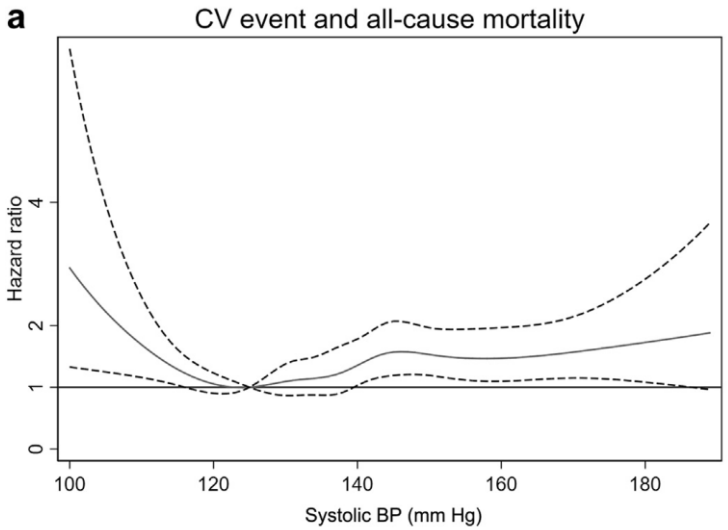


Figure 2: Cumulative incidence of chronic kidney disease with intensive and standard systolic blood pressure interventions in SPRINT and the ACCORD trial

Est-ce que le contrôle de l'HTA est important dans la MRC et pourquoi?

- Et dans les stades plus avancées?
  - Pas grand choses, une jolie observationnelle taiwanaise 2441 patients 40% de diabétique, DFG median 27,6 tous traités par antihypertenseurs. Suivi médian de 5 ans





Kidney International (2020) 97, 402–413

HTA et MRC: l'œuf ou la poule

- La MRC est responsable de l'HTA et explique en partie ainsi l'augmentation du risque cardiovasculaire
- Le niveau de preuve de la néphropathie hypertensive est faible
- Un contrôle tensionnel intensif ne dégage un bénéfice que pour les patients protéinuriques sur la fonction rénale
- Un contrôle tensionnel agressif pourrait dégagé un bénéfice en terme de mortalité en cas de MRC.

Les objectifs de pression artérielle en MRC

- Pour prévenir la dégradation de la fonction rénale
  - Si protéinurie, <125/75 mm Hg probablement intéressant
  - Si pas de protéinurie peut être risqué de trop bien contrôler
- Pour prévenir la mortalité
  - Stade 3 <130/80 mm Hg à conseiller
  - Stade 4 et 5, niveau de preuve faible éviter de passer sous les 120 de systolique
- De façon pragmatique: entre 120 et 140 mm Hg de systolique c'est bien.

Comment on fait ?

- Etape 1, faire le bilan des autres facteurs de risque cardiovasculaire

COR	LOE	Recommendation
I	B-NR	1. Screening for and management of other modifiable CVD risk factors are recommended in adults with hypertension.[S2.4-1,S2.4-2]

Modifiables	Non ou difficilement modifiables
Tabagisme actif ou passif	**MRC (DFG et albuminurie)**
Diabète	Antécédents familiaux
Hypercholestérolémie	Niveau socio-économique et éducationnel bas
Surpoids/obésité	Sexe masculin
Inactivité physique	**Syndrome apnée du sommeil**
Alimentation non saine	Stress psychologique

Comment on fait ?

- Etape 2: identifier des facteurs environnementaux
  - Surpoids et obésité
  - Régime riche en sel
  - Régime pauvre en potassium
  - Activité physique
  - Alcool

Comment on fait?

- Etape 3: les médicaments

Substances	Actions
Alcool	<1 chez les femmes et <2 hommes
Antidepresseurs (IMAO, IRSN, Tricycliques)	Chercher alternative IRS
Amphétamines	On arrête
Antipsychotiques atypiques (clozapine, olanzapine)	Alternative si possible
Caféine	Pas en comprimés
Décongestionnants	A bannir (lavage de nez)
Herbes (Ma huang, millepertuis, etc)	A bannir
Ciclosporine et tacrolimus	Alternative ou dosage
Contraceptifs oraux	A bannir ou alternative
AINS	A bannir
Drogues récréatives (bath salts et cocaïne)	A bannir
Corticoides	Dose la plus faible possible
Antiangiogénique et ITK	Bénéfice

Comment on fait?

- Pourquoi ne pas recommander le dépistage des sténoses des artères rénales?

Recommendations for Renal Artery Stenosis References that support recommendations are summarized in Online Data Supplements 7 and 24.		
COR	LOE	Recommendations
I	A	1. Medical therapy is recommended for adults with atherosclerotic renal artery stenosis.[S5.4.3-1,S5.4.3-2]

- Le café c'est bon: diminution de 2% du risque HTA par ajout d'une tasse/jour

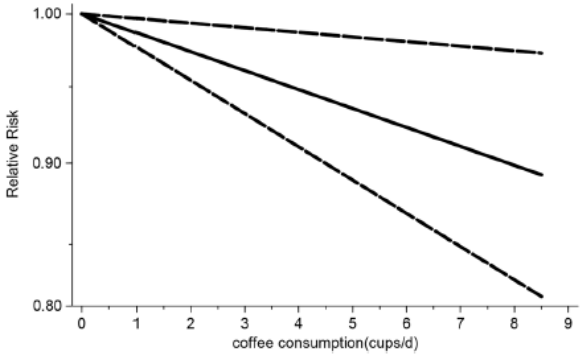


Fig. 4 Linear dose–response association between coffee consumption and hypertension modeled by using restricted cubic spline

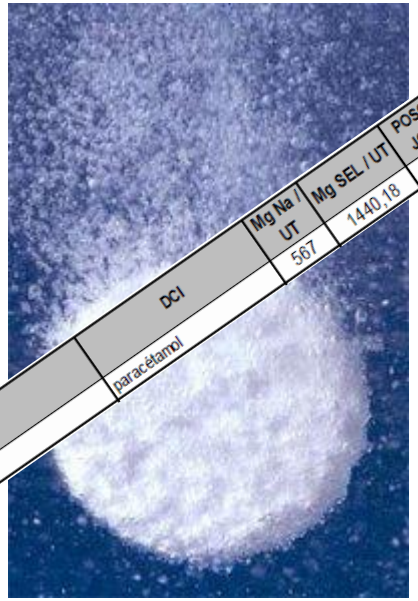
Journal of Human Hypertension (2018) 32:83–93

Comment on fait?

- Etape 4: les règles hygiénodiététiques 1A toutes

Intervention	Objectif	Impact	
		Hypertendu	Non hypertendu
Perte de poids	Diminution de 1 mm Hg par diminution de 1 Kg de poids	-5 mm Hg	-2/3 mm Hg
Régime DASH	Régime riche en fibres, fruits végétaux.	-11 mm Hg	-3 mm Hg
Régime limité en sodium	Moins de 1,5 g/jour (*2,5=4g) Réduire de 1 g déjà bien	-5/6 mm Hg	-2/3 mm Hg
Régime riche en potassium	Plus de 3,5g/jour	-4/5 mm Hg	-2 mm Hg
Exercice physique	Aérobie : 90-150 mn/semaine Resistance dynamique Resistance isométrique	-5/8 mm Hg	-2/4 mm Hg
Réduire sa consommation d'alcool	Homme<28 g/j Femme<14g/j	-4 mm Hg	-2 mm Hg

Où trouve-t-on du sel?



SPECIALITES	DCI	Mg Na / UT	Mg SEL / UT	POSO USUELLE JOURNALIERE	Grammes de SEL / J
EFFERALGAN 1 G CP EFF	paracétamol	567	1440,18	1-3/J	1,44-4,32

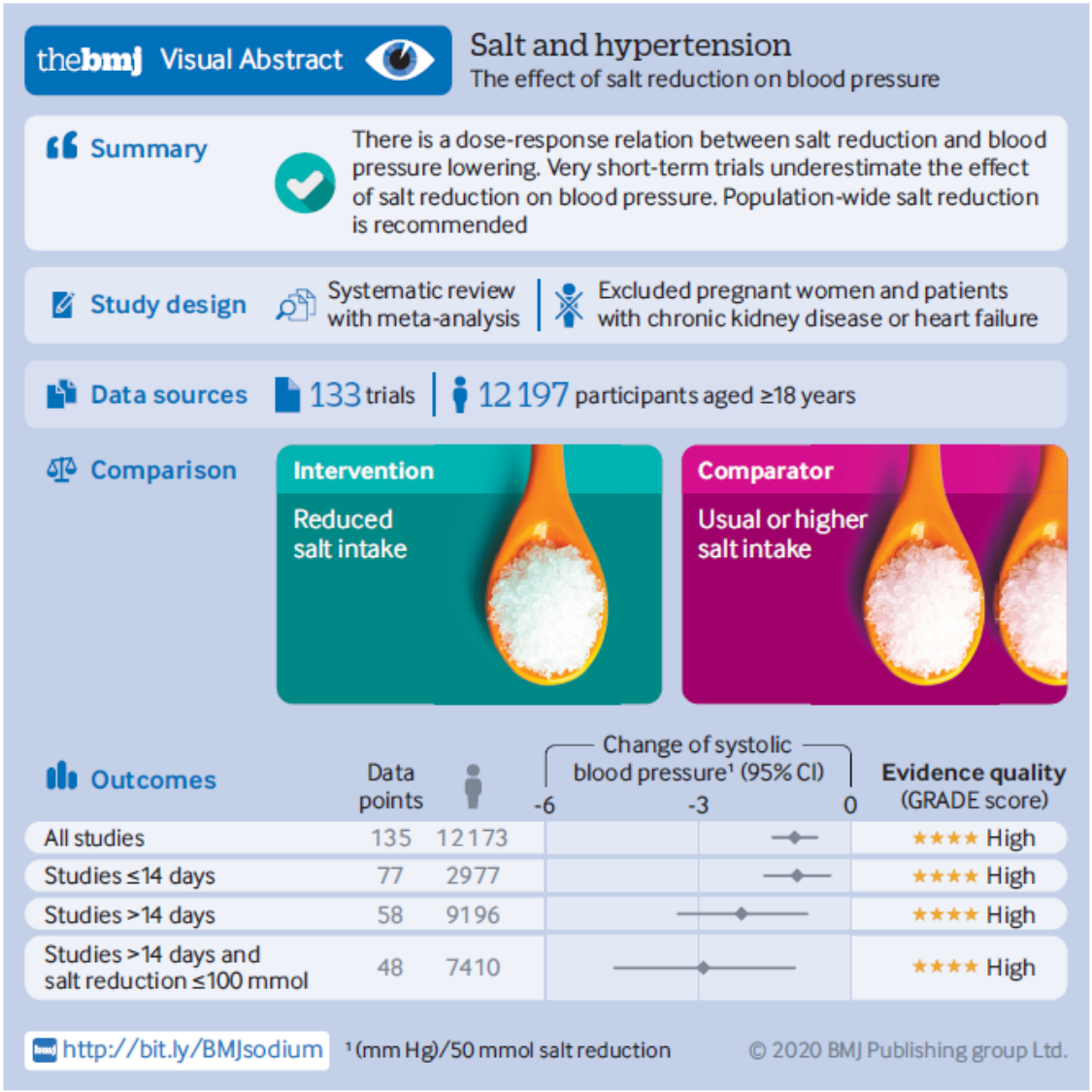
Produits	Quantité de sodium mg/100g
Charcuterie	2100
Saucisses de volaille	1000
Sardine à l'huile	760
Choucroute	650
Saumon fumé	1200
Haricot vert en conserve	410
Gruyère	420
Eau de Vichy	1600
Pain	500-650
Sauce soja	5717
Porc	60
Volaille	70
Sardine fraiche	70
Chou fleur	24
Saumon frais	48
Haricot vert frais	0
Lait de vache	50
Eau de Volvic	8
rhubarbe	3
Son d'avoine	3

14,5g

Où trouve-t-on du sel?

SPECIALITES	DCI	Mg Na / UT	Mg SEL / UT	POSO USUELLE JOURNALIERE	Grammes de SEL / J
ACETYLCYSTEINE BIOGARAN 200 MG CP EFF	acétylcystéine	114,9	291,846	3/J	0,87
ACETYLCYSTEINE GNR 200 MG CP EFF	acétylcystéine	600	1524	3/J	4,57
ACETYLCYSTEINE MERCK 200 MG CP EFF	acétylcystéine	165	419,1	3/J	1,26
AGRAM 500 MG CP EFF	amoxicilline	160	406,4	1-6/J	0,41-2,44
AMMONAPS 500 MG CP	phénylbutyrate de sodium	62	157,48	9,9-13 g/m²/j	3,15-6,30
AMMONAPS GRANULES	phénylbutyrate de sodium	124	314,96	9,9-13 g/m²/j	3,15-6,30
ANCOTIL 2,5 G INJ	flucytosine	792,32	2012,5	100-200 mg/kg/j	4,02-10,05
APACEF 1 G INJ	céfotetan	80	203,2	2-6/j	0,41-1,22
ASPIRINE UPSA 1 G CP EFF	acide acétylsalicylique	460	1168,4	1-6/J	1,17-7,01
ASPIRINE UPSA 500 MG CP EFF	acide acétylsalicylique	460	1168,4	1-12/J	1,17-14,02
ASPIRINE UPSA VIT C CP EFF	acide acétylsalicylique	485	1231,9	1-12/J	1,23-14,78
AZANTAC 150 MG CP EFF	ranitidine	328	833,12	1-4/J	0,83-3,33
AZANTAC 150 MG GRANULES EFF SACHET	ranitidine	235	596,9	1-4/J	0,60-2,39
AZANTAC 300 MG CP EFF	ranitidine	479	1216,66	1-2/J	1,22-2,44
AZANTAC 300 MG GRANULES EFF SACHET	ranitidine	235	596,9	1-2/J	0,60-1,20
AZANTAC 75 MG CP EFF	ranitidine	164	416,56	1-2/J	0,42-0,84
BAYPEN 5 G INJ	mezlocilline	213	541,02	240-300 mg/kg/j	1,62-2,70
BIODALGIC 50 MG CP EFF	tramadol	214	543,56	1-8/J	0,54-4,35
CALCIUM SANDOZ 500 MG CP EFF	calcium	275	698,5	2/J	1,40
CEPHALGAN PDR ORALE EFF SACHET	acide acétylsalicylique	119	302,26	1-3/J	0,30-0,90
CIMETIDINE MERCK 200 MG CP EFF	cimétidine	209	530,86	1-4/J	0,53-2,12
CIMETIDINE RPG 800 MG CP EFF	cimétidine	423	1074,42	1-2/J	1,07-2,14
CITRATE DE BETAINE 2G CP EFF	bétaine	450	1143	1-3/J	1,14-3,43
CITROCHOLINE AMP BUV	citrate de choline	100	254	1-3/J	0,25-0,76
CITROCHOLINE PDR ORALE SACHET	citrate de choline	250	635	1-3/J	0,63-1,90
CLAMOXYL 1 G INJ	amoxicilline	62,5	158,75	2-12/J	0,32-1,91
CLAMOXYL 2 G INJ	amoxicilline	125,8	319,532	1-6/J	0,32-1,91
CLARADOL 500 MG CP EFF	paracétamol	422	1071,88	1-6/J	1,07-6,42
CLARADOL CAFEINE CP EFF	paracétamol + caféine	422	1071,88	1-6/J	1,07-6,42
CLARAGINE 500 MG CP EFF	acide acétylsalicylique	255	647,7	1-6/J	0,65-3,90
CLAVENTIN 3 G INJ	ticarcilline + ac clavulanique	360	914,4	4-5/J	3,66-4,57
CLAVENTIN 5 G INJ	ticarcilline + ac clavulanique	600	1524	3/J	4,57
DOLIPRANE 1 G CP EFF	paracétamol	408	1036,32	1-3/J	1,04-3,12
DOLIPRANE 500 MG CP EFF	paracétamol	408	1036,32	1-6/J	1,04-6,24

Sel et HTA


thebmj Visual Abstract
Salt and hypertension
The effect of salt reduction on blood pressure
Summary
There is a dose-response relation between salt reduction and blood pressure lowering. Very short-term trials underestimate the effect of salt reduction on blood pressure. Population-wide salt reduction is recommended
Study design
Systematic review with meta-analysis
Excluded pregnant women and patients with chronic kidney disease or heart failure
Data sources
133 trials
12 197 participants aged ≥18 years
Comparison
Intervention
Reduced salt intake
Comparator
Usual or higher salt intake
Outcomes
Data points
Change of systolic blood pressure¹ (95% CI)
-6
-3
0
Evidence quality (GRADE score)
All studies 135 12173 ★★★★ High
Studies ≤14 days 77 2977 ★★★★ High
Studies >14 days 58 9196 ★★★★ High
Studies >14 days and salt reduction ≤100 mmol 48 7410 ★★★★ High
http://bit.ly/BMJsodium
¹(mm Hg)/50 mmol salt reduction
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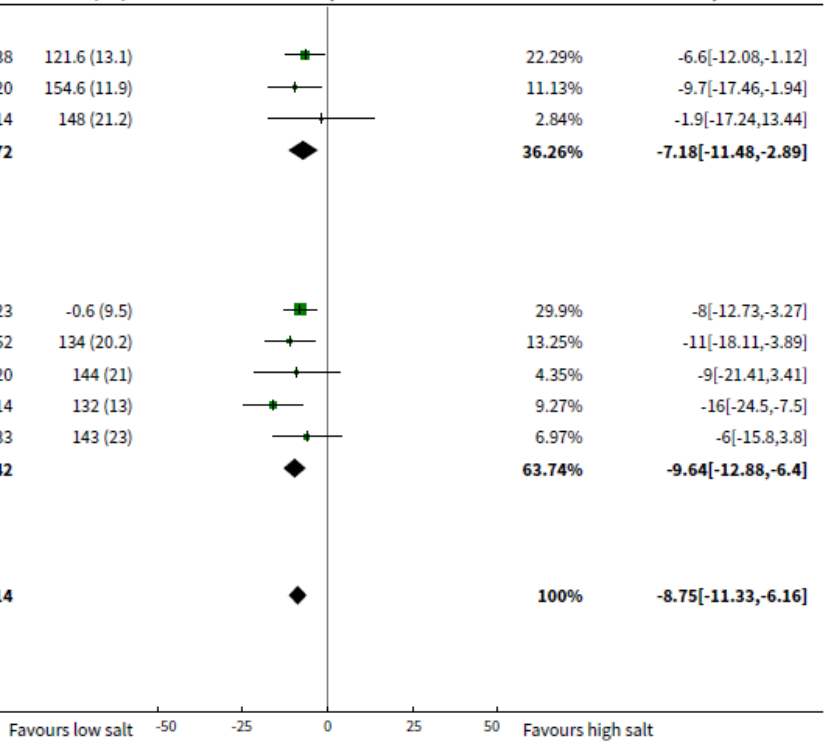
Sel, HTA et MRC

- Ca marche sur la tension artérielle, une réduction de 6g/j de NaCl c'est un médicament

Analysis 1.2. Comparison 1 Net change with altering salt and change by duration, Outcome 2 Systolic blood pressure.

Study or subgroup	Low salt N	Low salt Mean(SD)	High salt N	High salt Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.2.1 Short-term (< 4 weeks)							
Konishi 2001	38	115 (11.2)	38	121.6 (13.1)		22.29%	-6.6[-12.08,-1.12]
LowSALT CKD Study 2012	20	144.9 (13.1)	20	154.6 (11.9)		11.13%	-9.7[-17.46,-1.94]
Ruilope 1992a	14	146.1 (20.2)	14	148 (21.2)		2.84%	-1.9[-17.24,13.44]
Subtotal ***	**72**		**72**			**36.26%**	**-7.18[-11.48,-2.89]**
Heterogeneity: Tau²=0; Chi²=0.9, df=2(P=0.64); I²=0%							
Test for overall effect: Z=3.28(P=0)							
1.2.2 Long-term (≥ 4 weeks)							
de Brito-Ashurst 2013	25	-8.6 (6.9)	23	-0.6 (9.5)		29.9%	-8[-12.73,-3.27]
DUAAAL Study 2011	52	123 (16.6)	52	134 (20.2)		13.25%	-11[-18.11,-3.89]
Fine 1997	20	135 (19)	20	144 (21)		4.35%	-9[-21.41,3.41]
Keven 2006	18	116 (11)	14	132 (13)		9.27%	-16[-24.5,-7.5]
Vogt 2008	33	137 (17.2)	33	143 (23)		6.97%	-6[-15.8,3.8]
Subtotal ***	**148**		**142**			**63.74%**	**-9.64[-12.88,-6.4]**
Heterogeneity: Tau²=0; Chi²=3.29, df=4(P=0.51); I²=0%							
Test for overall effect: Z=5.83(P<0.0001)							
Total ***	**220**		**214**			**100%**	**-8.75[-11.33,-6.16]**
Heterogeneity: Tau²=0; Chi²=5, df=7(P=0.66); I²=0%							
Test for overall effect: Z=6.63(P<0.0001)							
Test for subgroup differences: Chi²=0.8, df=1 (P=0.37), I²=0%							



McMahon EJ, Campbell KL, Bauer JD, Mudge DW.
Altered dietary salt intake for people with chronic kidney disease.
Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD010070.
DOI: 10.1002/14651858.CD010070.pub2.

Une alternative

A randomized trial comparing the safety, adherence and pharmacodynamics profiles of two doses of sodium bicarbonate in CKD: The BASE Pilot Trial.

BASE

METHODS

CKD & tCO_2 20-28 (n=194)

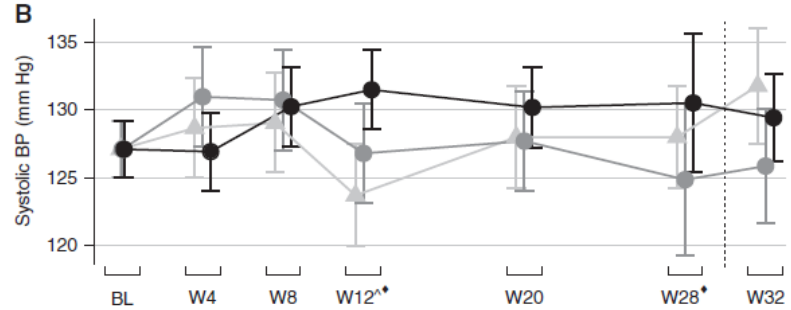
OUTCOMES

	Safe	Tolerable	BP	Weight	Serum tCO_2	Urinary NH_4^+	Urinary ACR
$NaHCO_3$ 0.8 meq/kg-LBW/d (n=90)	✓	✓	No Δ	No Δ	↑ 1.4 meq/L	↓↓	Modest ↑
$NaHCO_3$ 0.5 meq/kg-LBW/d (n=52)	✓	✓	No Δ	No Δ	↑ 0.1 meq/L	↓	Mild ↑
Placebo (n=52)	Reference Group						

CONCLUSION Both $NaHCO_3$ doses were safe and tolerable. Neither increased BP or weight. The higher dose raised serum bicarbonate and lowered urinary ammonium more than the lower dose. ACR increased in both groups, but the magnitude was greater with the higher dose.

doi: 10.1681/ASN.2019030287

ASN THE AMERICAN SOCIETY OF NEPHROLOGY



Sel, HTA et MRC

- Ca marche sur la protéinurie, pas de données concluante sur le DFG

Table 1. Measurement of urinary protein in included studies

Study	Proteinuria measurement	High salt	Low salt	Reduc-tion	Signifi-cance
DUAAAL Study 2011	Protein; geometric mean (95% CI) mg/d; 24 hour urine	1680 (1310 to 2140)	850 (660 to 1100)	49%	P < 0.001
	Protein to creatinine ratio; geometric mean (95% CI) mg/mg	1.2 (0.9 to 1.5)	0.6 (0.4 to 0.8)	51%	P < 0.01
Konishi 2001	Protein; median (IQR) mg/d; 24 hour urine	509 (207 to 1916)	372 (142 to 1134)	27%	P = 0.004
LowSALT CKD Study 2012	Protein; median (IQR) mg/d; 24 hour urine	835 (185 to 1600)	493 (123 to 1300)	40%	P < 0.01
	Albumin; median (IQR) mg/d; 24 hour urine	291 (40 to 1000)	143 (16 to 889)	51%	P < 0.001
	Protein: creatinine; median (IQR) g/mol creatinine; 24 hour urine	68 (23 to 164)	41 (17 to 126)	60%	P < 0.05
	Albumin:creatinine median (IQR) g/mol creatinine; 24 hour urine	27 (5 to 127)	9 (2 to 82)	67%	P < 0.05
Vogt 2008	Protein; mean (SE) mg/d; 24 hour urine	3800 (400)	3000 (300)	21%	P < 0.05
	Protein concentration; mean (SE) ng/mL	591 (78)	518 (85)	12%	P < 0.05
	Protein to creatinine ratio; mean (SE) mg/mg	2.45 (0.27)	2.10 (0.36)	14%	P < 0.05

Comment on fait?

- Etape 5: Un peu de paraclinique de base

Table 17. Basic and Optional Laboratory Tests for Primary Hypertension

Basic testing	Fasting blood glucose*
	Complete blood count
	Lipid profile
	Serum creatinine with eGFR*
	Serum sodium, potassium, calcium*
	Thyroid-stimulating hormone
	Urinalysis
	Electrocardiogram
Optional testing	Echocardiogram
	Uric acid
	Urinary albumin to creatinine ratio

*May be included in a comprehensive metabolic panel.
eGFR indicates estimated glomerular filtration rate.

Table 14 Routine workup for evaluation of hypertensive patients

Routine laboratory tests
Haemoglobin and/or haematocrit
Fasting blood glucose and glycated HbA_{1c}
Blood lipids: total cholesterol, LDL cholesterol, HDL cholesterol
Blood triglycerides
Blood potassium and sodium
Blood uric acid
Blood creatinine and eGFR
Blood liver function tests
Urine analysis: microscopic examination; urinary protein by dip-stick test or, ideally, albumin:creatinine ratio
12-lead ECG

eGFR = estimated glomerular filtration rate; ECG = electrocardiogram; HbA_{1c} = haemoglobin A1c.

©ESC/ESH 2018

Comment on fait?

- Etape 6: on évalue le risque CV, en pratique MRC = haut risque= médicament d'emblée

http://tools.acc.org/ASCVD-Risk-EstimatorPlus/#!/calculate/estimate/

Hypertension disease staging	Other risk factors, HMOD, or disease	BP (mmHg) grading			
		High normal SBP 130–139 DBP 85–89	Grade 1 SBP 140–159 DBP 90–99	Grade 2 SBP 160–179 DBP 100–109	Grade 3 SBP ≥180 or DBP ≥110
Stage 1 (uncomplicated)	No other risk factors	Low risk	Low risk	Moderate risk	High risk
	1 or 2 risk factors	Low risk	Moderate risk	Moderate to high risk	High risk
	≥3 risk factors	Low to Moderate risk	Moderate to high risk	High Risk	High risk
Stage 2 (asymptomatic disease)	HMOD, CKD grade 3, or diabetes mellitus without organ damage	Moderate to high risk	High risk	High risk	High to very high risk
Stage 3 (established disease)	Established CVD, CKD grade ≥4, or diabetes mellitus with organ damage	Very high risk	Very high risk	Very high risk	Very high risk

©ESC/ESH 2018

Comment on fait

- Etape 7: recommandations US

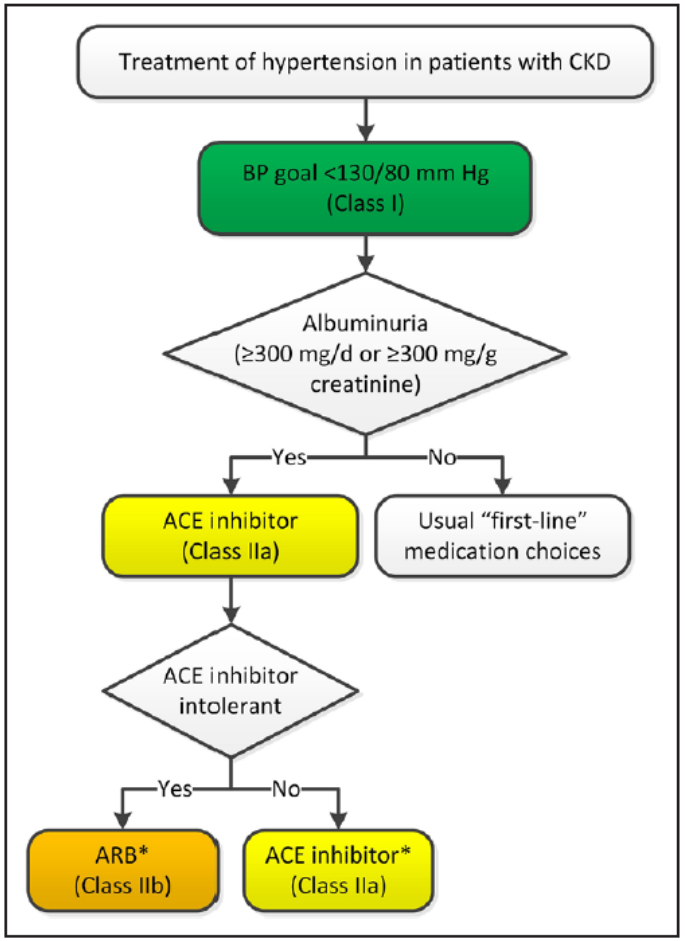


Figure 6. Management of hypertension in patients with CKD.

Recommendations for Treatment of Hypertension in Patients With CKD

References that support recommendations are summarized in Online Data Supplements 37 and 38 and Systematic Review Report.

COR	LOE	Recommendations
I	SBP: B-R[SR] DBP: C-EO	1. Adults with hypertension and CKD should be treated to a BP goal of less than 130/80 mm Hg.[S9.3-1–S9.3-6]
IIa	B-R	2. In adults with hypertension and CKD (stage 3 or higher or stage 1 or 2 with albuminuria [≥300 mg/d, or ≥300 mg/g albumin-to-creatinine ratio or the equivalent in the first morning void]), treatment with an ACE inhibitor is reasonable to slow kidney disease progression.[S9.3-3,S9.3-7–S9.3-12]
IIb	C-EO	3. In adults with hypertension and CKD (stage 3 or higher or stage 1 or 2 with albuminuria [≥300 mg/d, or ≥300 mg/g albumin-to-creatinine ratio in the first morning void]) (S9.3-7,S9.3-8), treatment with an ARB may be reasonable if an ACE inhibitor is not tolerated.

SR indicates systematic review.

Comment on fait?

- Etape 7: recommandations Européennes

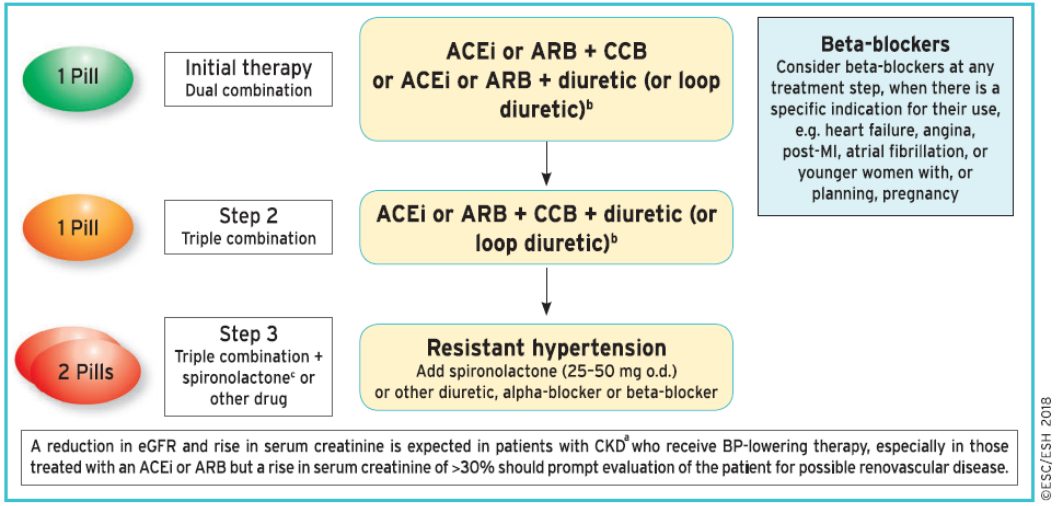


Figure 6 Drug treatment strategy for hypertension and chronic kidney disease. ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BP = blood pressure; CCB = calcium channel blocker; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; MI = myocardial infarction; o.d. = omni die (every day).

European Heart Journal (2018) **39**, 3021–3104

Therapeutic strategies for treatment of hypertension i CKD

Recommendations	Class[a]	Level[b]
In patients with diabetic or non-diabetic CKD, it is recommended that an office BP of ≥140/90 mmHg be treated with lifestyle advice and BP-lowering medication.[9,203,485]	I	A
In patients with diabetic or non-diabetic CKD: • It is recommended to lower SBP to a range of 130–139 mmHg.[9,487,489]	I	A
• Individualized treatment should be considered according to its tolerability and impact on renal function and electrolytes.	IIa	C
RAS blockers are more effective at reducing albuminuria than other antihypertensive agents, and are recommended as part of the treatment strategy in hypertensive patients in the presence of microalbuminuria or proteinuria.[487,489]	I	A
A combination of a RAS blocker with a CCB or a diuretic[c] is recommended as initial therapy.[175]	I	A
A combination of two RAS blockers is not recommended.[298]	III	A

Comment on fait?

- En pratique
  - Toujours règles hygiéno-diététiques
  - La bithérapie d'emblée est à privilégier et une association IEC-diurétique en premier.
  - L'objectif tensionnel est à moduler en fonction du patient.
    - <140 mm Hg dans tous les cas
    - <130 mm Hg quand protéinurie ou très haut risque CV
    - >120 mm Hg toujours
  - On favorise la monoprise (observance) le soir
  - Importance d'avoir des traitements couvrants l'ensemble du nycthémère

Choix de la molécule

Table 18. Oral Antihypertensive Drugs

Class	Drug	Usual Dose, Range (mg/d)*	Daily Frequency	Comments
Primary agents				
Thiazide or thiazide-type diuretics	Chlorthalidone	12.5–25	1	Chlorthalidone is preferred on the basis of prolonged half-life and proven trial reduction of CVD. Monitor for hyponatremia and hypokalemia, uric acid and calcium levels. Use with caution in patients with history of acute gout unless patient is on uric acid–lowering therapy.
	Hydrochlorothiazide	25–50	1	
	Indapamide	1.25–2.5	1	
	Metolazone	2.5–5	1	
ACE inhibitors	Benazepril	10–40	1 or 2	Do not use in combination with ARBs or direct renin inhibitor. There is an increased risk of hyperkalemia, especially in patients with CKD or in those on K^+ supplements or K^+-sparing drugs. There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis. Do not use if patient has history of angioedema with ACE inhibitors. Avoid in pregnancy.
	Captopril	12.5–150	2 or 3	
	Enalapril	5–40	1 or 2	
	Fosinopril	10–40	1	
	Lisinopril	10–40	1	
	Moexipril	7.5–30	1 or 2	
	Perindopril	4–16	1	
	Quinapril	10–80	1 or 2	
	Ramipril	2.5–20	1 or 2	
	Trandolapril	1–4	1	
ARBs	Azilsartan	40–80	1	Do not use in combination with ACE inhibitors or direct renin inhibitor. There is an increased risk of hyperkalemia in CKD or in those on K^+ supplements or K^+-sparing drugs. There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis. Do not use if patient has history of angioedema with ARBs. Patients with a history of angioedema with an ACE inhibitor can receive an ARB beginning 6 weeks after ACE inhibitor is discontinued. Avoid in pregnancy.
	Candesartan	8–32	1	
	Eprosartan	600–800	1 or 2	
	Irbesartan	150–300	1	
	Losartan	50–100	1 or 2	
	Olmesartan	20–40	1	
	Telmisartan	20–80	1	
	Valsartan	80–320	1	
CCB—dihydropyridines	Amlodipine	2.5–10	1	Avoid use in patients with HFrEF; amlodipine or felodipine may be used if required. They are associated with dose-related pedal edema, which is more common in women than men.
	Felodipine	2.5–10	1	
	Isradipine	5–10	2	
	Nicardipine SR	60–120	2	
	Nifedipine LA	30–90	1	
	Nisoldipine	17–34	1	
CCB—nondihydropyridines	Diltiazem ER	120–360	1	Avoid routine use with beta blockers because of increased risk of bradycardia and heart block. Do not use in patients with HFrEF. There are drug interactions with diltiazem and verapamil (*CYP3A4* major substrate and moderate inhibitor).
	Verapamil IR	120–360	3	
	Verapamil SR	120–360	1 or 2	
	Verapamil-delayed onset ER	100–300	1 (in the evening)	

- Utiliser des molécules en prise unique
- Le loxen est un mauvais antihypertenseur
  - Tachycardisant
  - CI dans l'insuffisance cardiaque et la coronaropathie
  - Favorise les OAP

Choix de la molécule

Secondary agents				
Diuretics—loop	Bumetanide	0.5–2	2	These are preferred diuretics in patients with symptomatic HF. They are preferred over thiazides in patients with moderate-to-severe CKD (eg, GFR <30 mL/min).
	Furosemide	20–80	2	
Diuretics—aldosterone antagonists	Eplerenone	50–100	1 or 2	These are preferred agents in primary aldosteronism and resistant hypertension. Spironolactone is associated with greater risk of gynecomastia and impotence as compared with eplerenone. This is common add-on therapy in resistant hypertension. Avoid use with K^+ supplements, other K^+-sparing diuretics, or significant renal dysfunction. Eplerenone often requires twice-daily dosing for adequate BP lowering.
	Spironolactone	25–100	1	
Beta blockers—cardioselective	Atenolol	25–100	2	Beta blockers are not recommended as first-line agents unless the patient has IHD or HF. These are preferred in patients with bronchospastic airway disease requiring a beta blocker. Bisoprolol and metoprolol succinate are preferred in patients with HF/EF. Avoid abrupt cessation.
	Betaxolol	5–20	1	
	Bisoprolol	2.5–10	1	
	Metoprolol tartrate	100–200	2	
	Metoprolol succinate	50–200	1	
Beta blockers—cardioselective and vasodilatory	Nebivolol	5–40	1	Nebivolol induces nitric oxide–induced vasodilation. Avoid abrupt cessation.

- Utiliser des molécules en prise unique
- L'atenolol est à éviter
- Les bétabloquants si pas insuffisance cardiaque ou de coronaropathie sont en dernière position
- Alpha bloquant: pour la prostate

Tuons une idée reçue

- Les thiazidiques marchent dans l'insuffisance rénale chronique même sévère

A Randomized Trial of Distal Diuretics *versus* Dietary Sodium Restriction for Hypertension in Chronic Kidney Disease

METHODS

- 26 patients with CKD G3 or G4 + hypertension
- Randomized cross-over trial: amiloride/HCTZ (5/50 mg) *vs.* Na^+ restriction (60 mmol/day)
- Measurements: clinical parameters, fluid balance, diuretic clearance

OUTCOME

Parameter	Diuretics	Na^+ restriction
24h systolic BP, mm Hg	– 14	– 5
Body weight, kg	– 1.5	– 1.6
NT-pro-BNP, pmol/L	– 12	– 7
24h urine Na^+, mmol/d	– 1	– 95

CONCLUSIONS

- Distal diuretics are non-inferior to dietary Na^+ restriction in reducing blood pressure and extracellular volume in chronic kidney disease.
- Diuretic sensitivity is maintained at lower eGFR despite lower diuretic clearance.

JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

TABLE II. Fractional Excretions of Sodium and Chloride and Renal Parameters During the Study

	Basal State	FUR	HCTZ	Combined Regimen (FUR + HCTZ)[a]
FE Na^+	3.4±1.8	4.4±2.2	3.9±2.4	4.9±2.8[b]
FE Cl^-	3.8±2.0	5.1±2.9	4.6±2.5	6.0±3.1[b]
Mean blood pressure, mm Hg	101±13	93±9[b]	94±7[b]	86±13[c]
GFR, mL/min/1.73 m^2	25±10	21±10	22±10	18±11[c]
RPF, mL/min/1.73 m^2	95±35	96±31	94±36	85±41
RVR, mm Hg/mL/min/1.73 m^2	2.0±1.0	1.7±0.8	1.9±1.1	1.8±1.0
FF, %	27±8	22±6[b]	23±7[b]	20±6[c]

Abbreviations: FECl, fractional excretion of chloride; FE Na, fractional excretion of sodium; FF, filtration fraction; FUR, furosemide; GFR, glomerular filtration rate; HCTZ, hydrochlorothiazide; RPF, renal plasma flow; RVR, renal vascular resistance. [a]Only 16 patients were included in the analysis. [b]$P<.05$ vs basal. [c]$P<.01$ vs basal.

The Journal of Clinical Hypertension Vol 14 | No 1 | January 2012

Choix de l'inhibiteur calcique

- L'amlodipine avec ALLHAT est l'inhibiteur calcique de loin le mieux évalué dans l'HTA (une prise, demie vie de 35 à 50h)
- La nicardipine orale: à éviter absolument

Maladie cardiovasculaire ischémique

Le traitement par des dihydropyridines à courte durée d'action peut être associé à un risque accru d'événements cardiovasculaires ischémiques.

Insuffisance cardiaque

La nicardipine doit être utilisée avec précaution chez les patients atteints d'insuffisance cardiaque, en raison du risque d'aggravation de l'insuffisance cardiaque.

Œdème pulmonaire aigu lors de la grossesse

http://base-donnees-publique.medicaments.gouv.fr/affichageDoc.php?specid=69198890&typedoc=R

renal insufficiency (creatinine clearance ranging between 17 and 62 ml/min). After 1 year of treatment, these agents caused a similar decrease in blood pressure. Only enalapril, however, caused a significant decrease in UAE (from 641 +/- 98 to 292 +/- 47 mg/24 h, p less than 0.01), whereas UAE did not change in the group treated with nicardipine (675 +/- 78 vs. 601 +/- 75 mg/24 h). Creatinine

Am J Nephrol 1991;11:131–137

Pour mémoire

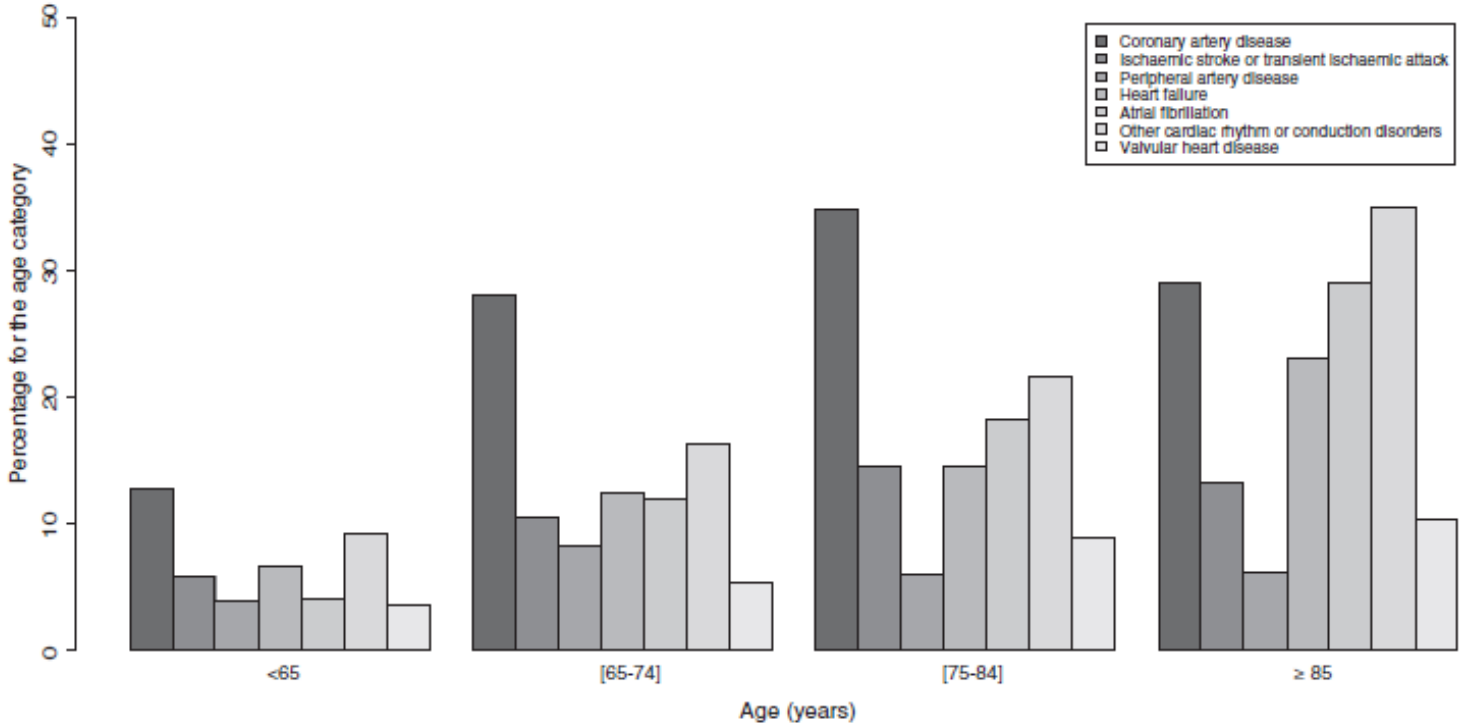


FIGURE 1: Prevalence of CVD by age group in 3033 patients with CKD.

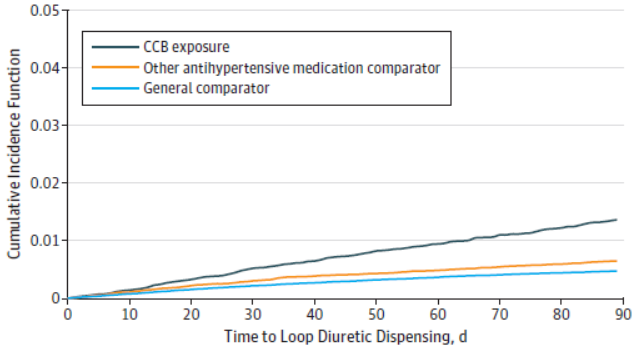
Nephrol Dial Transplant (2020) 35: 827–836
doi: 10.1093/ndt/gfy277

Le problème des dihydropyridines

- L'effet secondaire le plus limitant, les œdèmes
- Ils peuvent être majeurs et être responsable d'OAP.
- Plus fréquent au cours de la maladie rénale chronique
- Une preuve

JAMA Intern Med. doi:10.1001/jamainternmed.2019.7087
Published online February 24, 2020.

Figure. Cumulative Incidence of Being Dispensed a Loop Diuretic Among Older Adults With Hypertension Who Were Newly Dispensed a Calcium Channel Blocker (CCB) Compared With Other Antihypertensive Medication Comparators and General Comparators



No. at risk										
CCB exposure	40768	40009	39015	38292	28709	28176	27221	26221	25671	24889
Other antihypertensive medication comparator	65734	65202	64700	64268	63922	63588	63299	63001	62711	62450
General comparator	229565	226539	224451	222763	221329	220034	218840	217730	216719	215750

By 90 days, individuals newly dispensed a CCB had a higher cumulative incidence of receiving a loop diuretic (1.4%) compared with the other antihypertensive medication comparator group (0.7%) and the general comparator group (0.5%) ($P < .001$).

IEC vs Sartans

- IEC meilleur dans l'insuffisance cardiaque

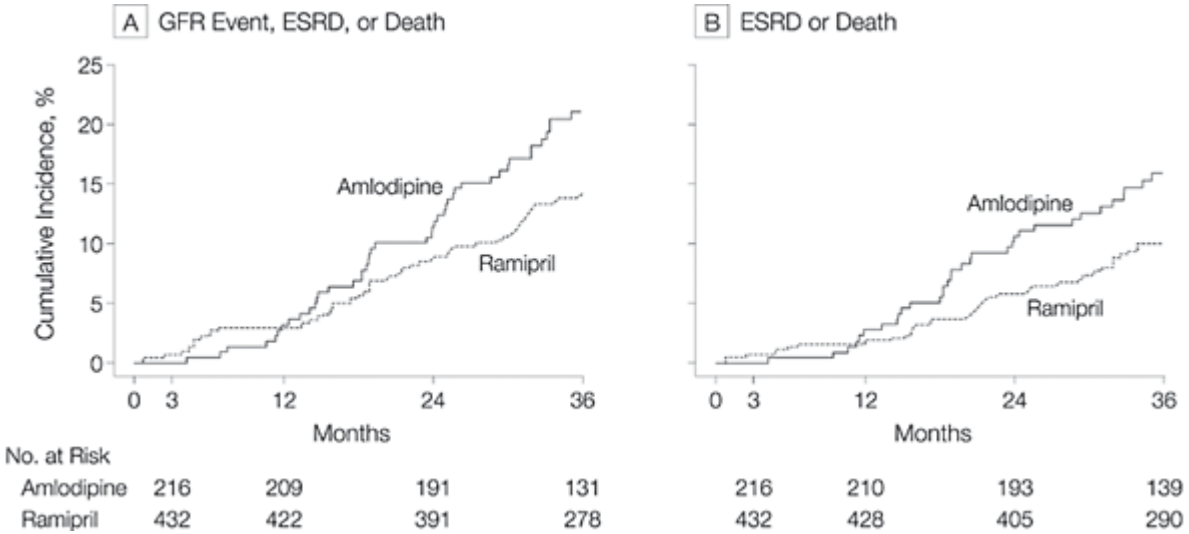
Table 4 Results of the comparisons of the network meta-analysis

Comparison	All-cause mortality	CV mortality	MI	Stroke	HF
ACEIs vs ARBs	0.96 (0.80–1.14)	0.87 (0.67–1.14)	1.02 (0.75–1.37)	1.13 (0.87–1.46)	0.71 (0.54–0.93)
ARBs vs placebo	0.90 (0.75–1.08)	0.91 (0.72–1.15)	0.90 (0.71–1.13)	0.80 (0.67–0.96)	1.05 (0.82–1.35)
ACEIs vs placebo	0.86 (0.75–0.99)	0.79 (0.62–1.01)	0.91 (0.74–1.11)	0.91 (0.75–1.09)	0.74 (0.66–0.83)

Data presented as risk ratio (RR) and its correspondent 95% confidence interval (CI)

Journal of Human Hypertension (2019) 33:188–201

- Les IEC c'est bon pour le rein



JAMA. 2001;285(21):2719-272

IEC vs Sartans

- Dans la néphropathie diabétique (2001)

Angiotensin II receptor blockers									
IDNT (irbesartan)	1,715 (66.5%/ 72.4%)	Age 58.9 years; SBP 159.0 mmHg; urinary protein excretion 2.9 g per 24 h; HbA_{1c} 8.2%	2.6	Reduction in proteinuria: −33% (P<0.001)/−10% (P=NA)	16.9%/23.7% (HR 0.67, 95% CI 0.52–0.87, P=0.003)	14.2%/17.8% (HR 0.77, 95% CI 0.57–1.03, P=0.07)	15.0%/16.3% (HR 0.92, 95% CI 0.69–1.23, P=0.57)	Mean arterial BP: −3.3 mmHg (P=0.001)	7
RENAAL (losartan)	1,513 (63.5%/ 48.6%)	Age 60 years; SBP 152.5 mmHg; median ACR 1,249 g/g; HbA_{1c} 8.5%	3.4	Proteinuria reduction: −35%/18% (P<0.001)	21.6%/26.0% (P=0.006)	19.6%/25.5% (P=0.002)	21.0%/20.3% (P=0.88)	Mean arterial BP: −0.4 mmHg (P=NS)	8

The investigated drugs were given in addition to the current standard of care therapy. ACR, albumin:creatinine ratio; BP, blood pressure; eGFR, estimated glomerular filtration rate; GLP1, glucagon-like peptide 1; HbA_{1c}, haemoglobin A_{1c}; NA, not available; NS, not significant; RRT, renal replacement therapy; SBP, systolic blood pressure; SGLT2, sodium–glucose cotransporter 2; T2DM, type 2 diabetes mellitus. *Data are means unless otherwise specified. ‡A composite outcome comprising doubling of serum creatinine levels accompanied by eGFR <45 ml/min/1.73 m².

- Vous choisissez la classe thérapeutique avec vous êtes le plus à l'aise.
- Indispensable dans une MRC avec protéinurie.

IEC et sartans

- Faut il en avoir peur après une insuffisance rénale aigue
  - 8558 IRA nécessitant la dialyse et hypertendu, 4,4 ans de suivi comparant bloqueur du SRAA et non usage après IRA.

TABLE 2. Multivariate Cox Regression Analysis of the Angiotensin-Converting Enzyme Inhibitor/Angiotensin II Receptor Blocker Use on Patient Outcomes

		95% CI				95% CI		
Outcomes	Crude HR	Lower	Upper	*p*	Adjusted HR[a]	Lower	Upper	*p*
End-stage renal disease	0.98	0.93	1.03	0.34	0.95	0.90	1.01	0.06
All-cause death[b]	0.92	0.87	0.97	0.03	0.93	0.87	0.98	0.011[c]
Malignancy death	0.77	0.67	0.89	< 0.001	0.82	0.70	0.95	0.010[c]
Infection death	0.83	0.67	1.03	0.09	0.84	0.66	1.05	0.13
Cardiovascular death	1.02	0.93	1.12	0.70	0.99	0.90	1.10	0.85
Accident death	0.86	0.74	0.99	0.038	0.87	0.74	1.02	0.09
Other death	0.94	0.84	1.05	0.30	1.01	0.89	1.14	0.86

HR = hazard ratio.
[a]The clustered Cox model was adjusted for age, gender, diabetes mellitus, coronary artery disease, congestive heart failure, prior stroke, chronic obstructive
nzyme inhibitor/angiotensin II receptor blocker or β-blocker use,
ics, thiazides), post-AKI use of antihypertensive drugs other than
calcium channel blockers), insulin, and statins, hospitalization days of the
replacement therapy (CRRT)/sustained low-efficiency daily dialysis use,
vascular, postsurgical, or intoxication).

Angiotensin-Converting Enzyme Inhibitors and or Receptor Blockers After Acute Kidney Injury: Rehabilitation of the Supervillains*

DOI: 10.1097/CCM.0000000000004588

HTA résistante

1. Vérifier que trithérapie adaptée (diurétique)
2. Vérifier la prise des médicaments (SFH)
   1. On discute, utilité des questionnaires
   2. Discuter des effets secondaires, du nombre de prises, de l'utilité, du nombre de médicaments etc
   3. Possibilité de dosage de certains
3. Vérifier en ambulatoire l'HTA
4. Facteurs de résistance
   1. Régime (limitation en sel)
   2. Médicaments (AINS et drogues récréatives)
   3. Alcool

Blocage du récepteur au minéralocorticoides

- C'est le add-one à utiliser quand l'HTA est résistante (IEC ou sartan, diurétique, anticalcique): spironolactone (25-50 mg/j). Pathway-2
- La limite, pas possible si <45ml/mn/1,73m2

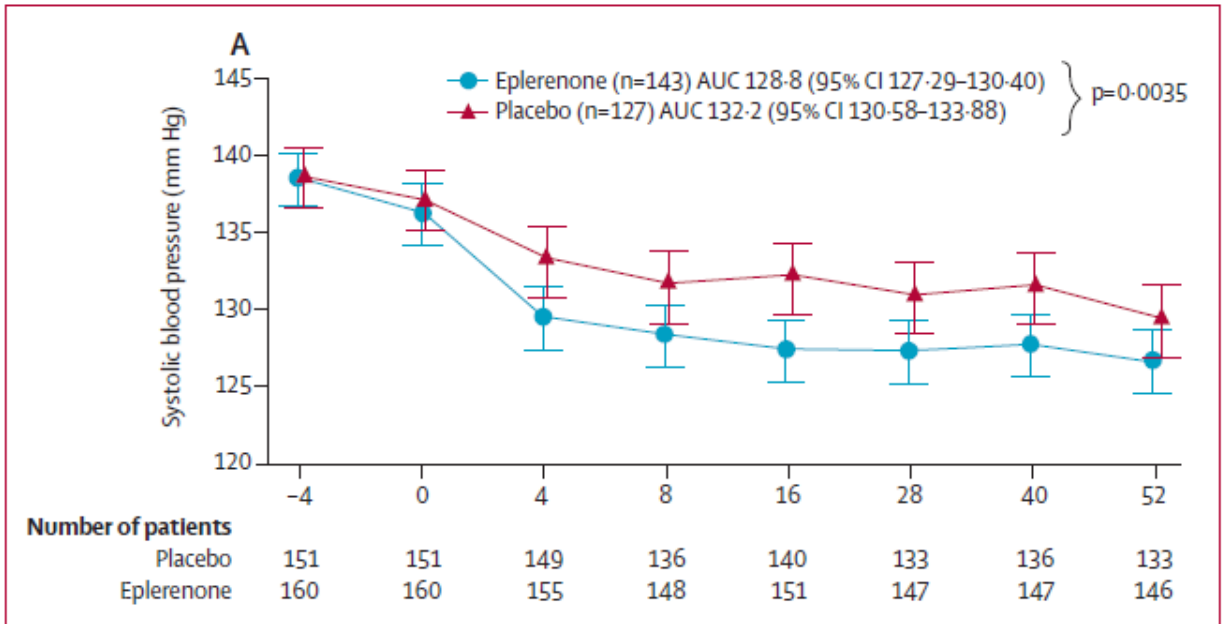
	Blood pressure (mm Hg)	Change from baseline (mm Hg)
Mean		
Spironolactone	133·5 (132·3 to 134·8)	−14·4 (−15·6 to −13·1)
Doxazosin	138·8 (137·6 to 140·1)	−9·1 (−10·3 to −7·8)
Bisoprolol	139·5 (138·2 to 140·8)	−8·4 (−9·7 to −7·1)
Placebo	143·7 (142·5 to 145·0)	−4·2 (−5·4 to −2·9)
Mean differences		
Spironolactone *vs* placebo	−10·2 (−11·7 to −8·74)	p<0·0001
Spironolactone *vs* mean bisoprolol and doxazosin	−5·64 (−6·91 to −4·36)	p<0·0001
Spironactone *vs* doxazosin	−5·30 (−6·77 to −3·83)	p<0·0001
Spironolactone *vs* bisoprolol	−5·98 (−7·45 to −4·51)	p<0·0001

Data are mean (95% CI). Sensitivity analysis using only the mean home systolic blood pressure at the final visit of each cycle (week 12).

Table 3: Home systolic blood pressure at final visit of each cycle

Blocage du récepteur au minéralocorticoides

- Si vous aimez pas la spironolactone, comme antihypertenseur l'eplerenone n'est pas la panacée, diminution de 5 mm Hg.



Blocage du récepteur au minéralocorticoides

- AMBER arriva
  - Est-ce que le patiromer permet de garder de la spironolactone? K<5,1 à l'inclusion et stop K>6 mmol/l

	Spironolactone and placebo (n=148)	Spironolactone and patiromer (n=147)
Age (years)*	68·5 (11·1)	67·8 (12·2)
<65	44 (30%)	49 (33%)
≥65	104 (70%)	98 (67%)
Sex		
Female	71 (48%)	71 (48%)
Male	77 (52%)	76 (52%)
Race		
White	145 (98%)	145 (99%)
Black	2 (1%)	2 (1%)
Other	1 (1%)	0
Weight (kg)	83·5 (14·4)	82·6 (15·5)
Diabetes	72 (49%)	73 (50%)
History of stroke or cerebrovascular accident	15 (10%)	14 (10%)
History of myocardial infarction	26 (18%)	31 (21%)
History of heart failure	69 (47%)	63 (43%)
History of atrial fibrillation	17 (11%)	11 (7%)
Number of antihypertensive medications		
Mean (SD)	3·6 (0·7)	3·7 (0·9)
Median (IQR)	3 (3–4)	4 (3–4)
Antihypertensive medications, n (%)		
β blockers	86 (58%)	87 (59%)
Calcium channel blockers	106 (72%)	107 (73%)
Diuretics	145 (98%)	146 (99%)
Renin angiotensin aldosterone system inhibitor	147 (99%)	147 (100%)
Other	31 (21%)	40 (27%)
Medications used for diabetes	68 (46%)	69 (47%)
Systolic automated office blood pressure (mm Hg)	144·9 (7·0)	143·3 (6·5)
Serum potassium (mmol/L)	4·69 (0·37)	4·74 (0·36)
<4·3	17 (11%)	7 (5%)
4·3 to <4·7	52 (35%)	55 (37%)
4·7 to 5·1	65 (44%)	65 (44%)
>5·1	14 (9%)	20 (145)
Estimated glomerular filtration rate (mL/min per 1·73 m²)	36·1 (7·6)	35·4 (7·3)
Serum creatinine (µmol/L)	151·6 (129·1–173·3)	150·3 (129·1–176·8)
24-h urine albumin to creatinine ratio (mg/g)	73·0 (18·8–400·0)	87·4 (18·4–466·7)
24-h urine sodium (mmol/24 h)	189·3 (142·0–234·9)	175·0 (119·9–258·0)

Data are mean (SD), n (%), or median (IQR). *At time of informed consent.

Table 1: **Baseline characteristics**

AMBER

- Le patiromer ne fait pas baisser la pression artérielle, la spironolactone oui… (12 semaines)

	Spironolactone and placebo (n=148)	Spironolactone and patiromer (n=147)	Difference between groups (95% CI)	p value for between-group difference
Primary endpoint				
Patients who remained on spironolactone at week 12	98 (66%)	126 (86%)	19·5% (10·0 to 29·0)	<0·0001
Secondary endpoint				
Systolic automated office blood pressure (mm Hg)	..	..	−1·0* (−4·4 to 2·4)	0·58
Baseline	144·9 (0·6)	143·3 (0·5)	..	..
Week 12	133·9 (1·4)	131·9 (1·2)	..	..
Change from baseline in systolic automated office blood pressure (mm Hg), least squares mean (95% CI)	−10·8 (−13·2 to −8·3)†	−11·7 (−14·1 to −9·3)‡	..	..
p value for change from baseline	<0·0001	<0·0001	..	..
Spironolactone dose				
Cumulative dose of spironolactone (mg)	2580·7 (95·8)	2942·3 (80·1)	384·7* (140·4 to 629·0)	0·0021

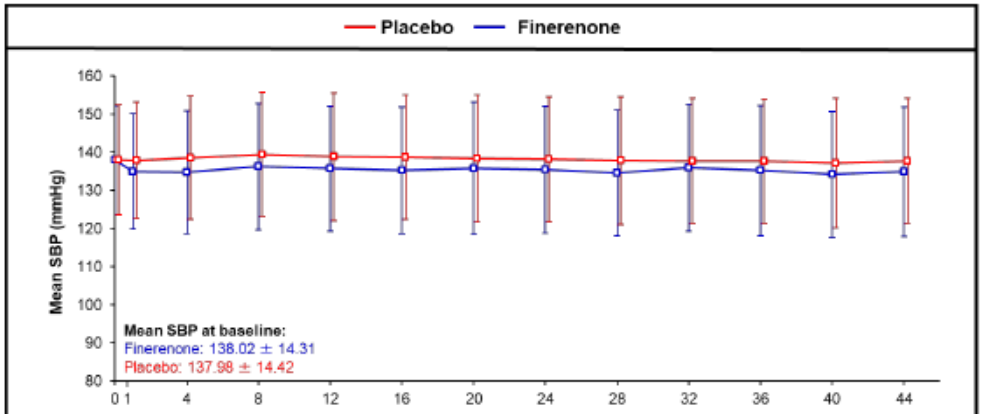
Data are n (%) or mean (SE), unless otherwise indicated. *Least squares mean. †n=141. ‡n=144.

Table 2: **Primary endpoint, secondary efficacy endpoint, and spironolactone dose**

Blocage du récepteur au minéralocorticoides

- Finerenone, un antagoniste non stéroidien du récepteur aux minéralocorticoides. (FIDELIO-DKD): 5764 patient diabétique avec DFG entre 25 et 75 et protéinurie, on the top de blocage maximum, 65 ans, DFG 44 ml/mn, UAC: 830.

Figure S7. Mean systolic blood pressure over time



No. of patients						
Finerenone	2826	2746	2628	1906	902	348
Placebo	2831	2751	2636	1895	884	353
Mean change in SBP from baseline (mmHg)						
Finerenone	Ref	-3.20	-2.13	-1.83	-2.58	-2.84
Placebo	Ref	0.68	0.87	0.38	-0.12	-0.08

FIDELIO-DKD

- Dose moyenne reçu est de 15 mg (10 ou 20)
- Suivi médian de 2,6 ans
- Kaliémie<4,8 mmol/l

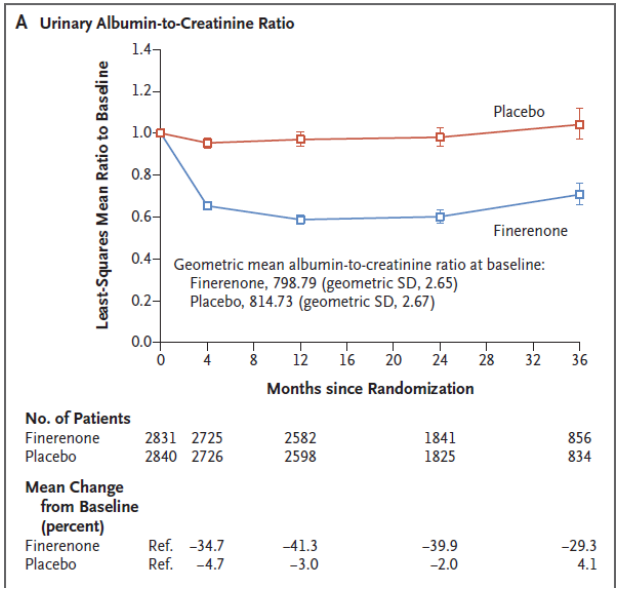
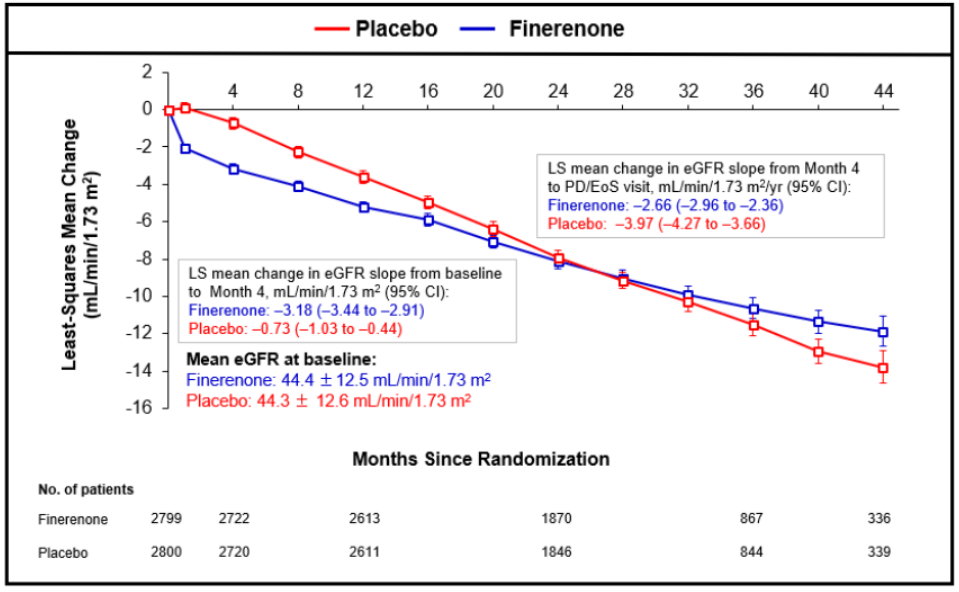
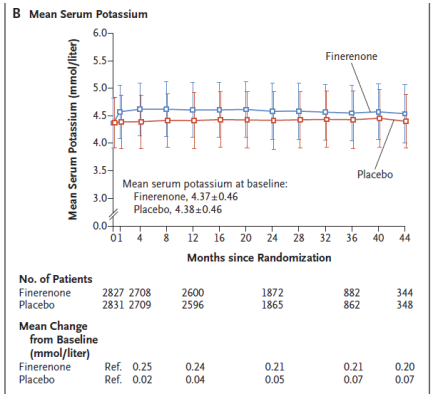


Figure S6. Effects of finerenone and placebo on eGFR





Fidelio DKD

- Les résultats peut être

Outcome	Finerenone (N=2833)	Placebo (N=2841)	Finerenone (N=2833)	Placebo (N=2841)	Hazard Ratio (95% CI)	P Value
	no. of patients with event (%)		*no. of patients with event per 100 patient-yr*			
Primary composite outcome	504 (17.8)	600 (21.1)	7.59	9.08	0.82 (0.73–0.93)	0.001
Kidney failure	208 (7.3)	235 (8.3)	2.99	3.39	0.87 (0.72–1.05)	—
End-stage kidney disease	119 (4.2)	139 (4.9)	1.60	1.87	0.86 (0.67–1.10)	—
Sustained decrease in eGFR to <15 ml/min/1.73 m^2	167 (5.9)	199 (7.0)	2.40	2.87	0.82 (0.67–1.01)	—
Sustained decrease of ≥40% in eGFR from baseline	479 (16.9)	577 (20.3)	7.21	8.73	0.81 (0.72–0.92)	—
Death from renal causes	2 (<0.1)	2 (<0.1)	—	—	—	—
Key secondary composite outcome	367 (13.0)	420 (14.8)	5.11	5.92	0.86 (0.75–0.99)	0.03
Death from cardiovascular causes	128 (4.5)	150 (5.3)	1.69	1.99	0.86 (0.68–1.08)	—
Nonfatal myocardial infarction	70 (2.5)	87 (3.1)	0.94	1.17	0.80 (0.58–1.09)	—
Nonfatal stroke	90 (3.2)	87 (3.1)	1.21	1.18	1.03 (0.76–1.38)	—
Hospitalization for heart failure	139 (4.9)	162 (5.7)	1.89	2.21	0.86 (0.68–1.08)	—
Death from any cause	219 (7.7)	244 (8.6)	2.90	3.23	0.90 (0.75–1.07)	—
Hospitalization for any cause	1263 (44.6)	1321 (46.5)	22.56	23.87	0.95 (0.88–1.02)	—
Secondary composite kidney outcome	252 (8.9)	326 (11.5)	3.64	4.74	0.76 (0.65–0.90)	—
Sustained decrease of ≥57% in eGFR from baseline	167 (5.9)	245 (8.6)	2.41	3.54	0.68 (0.55–0.82)	—

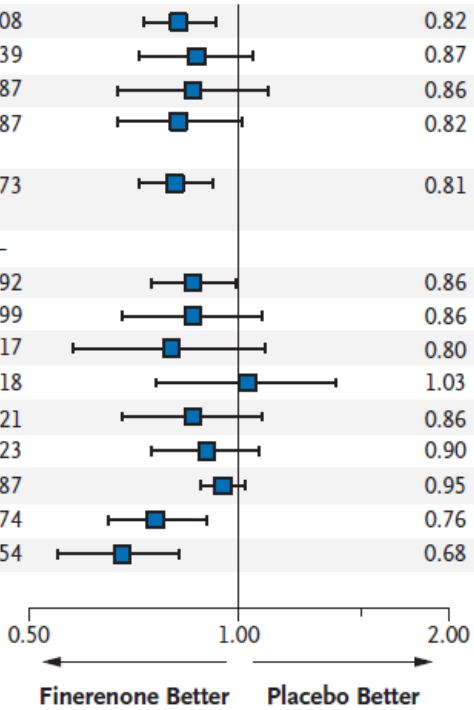


Figure 2. Efficacy Outcomes.

Antagonistes des minéralocorticoides

- Vous pouvez utiliser la spironolactone même à des stades avancés de la MRC pour traiter les HTA résistantes.
- Attention à la kaliémie (ne commencez pas si >5,1 mmol/l)
- L'ajout de chélateurs peut permettre d'éviter les hyperK
- La place de la finérenone va se poser.

Effets hypotenseurs des gliflozines

- Meta-analyse de plus de 28000 patients

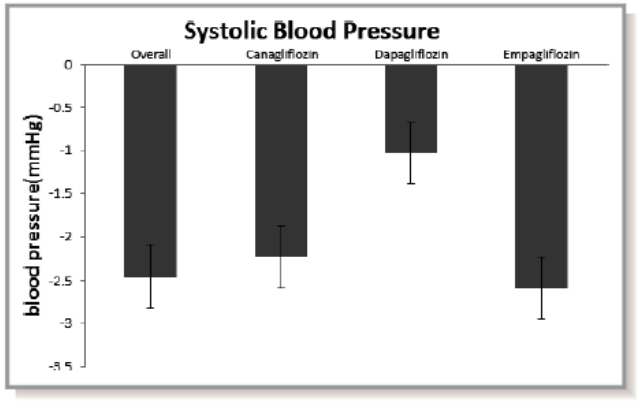


Figure 2. Plot to display weighted mean differences (bars) and 95% CIs (whiskers) for the impact of SGLT2 therapy on systolic blood pressure. SGLT 2, sodium-glucose cotransporter 2.

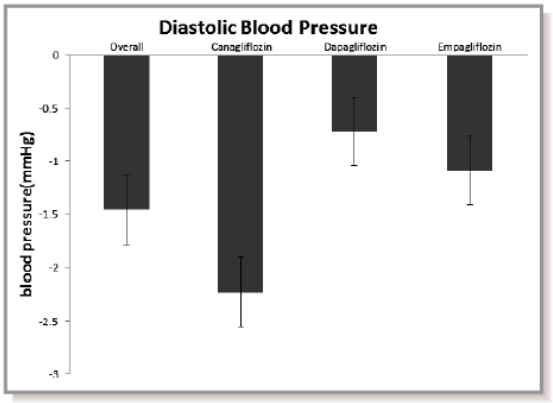
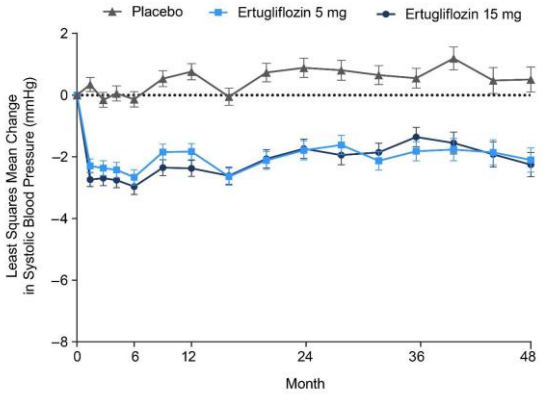


Figure 3. Plot to display weighted mean differences (bars) and 95% CIs (whiskers) for the impact of SGLT2 inhibitor therapy on diastolic blood pressure. SGLT 2, sodium-glucose cotransporter 2.

(*J Am Heart Assoc.* 2017;6:e004007.



Effets néphroprotecteurs des gliflozines

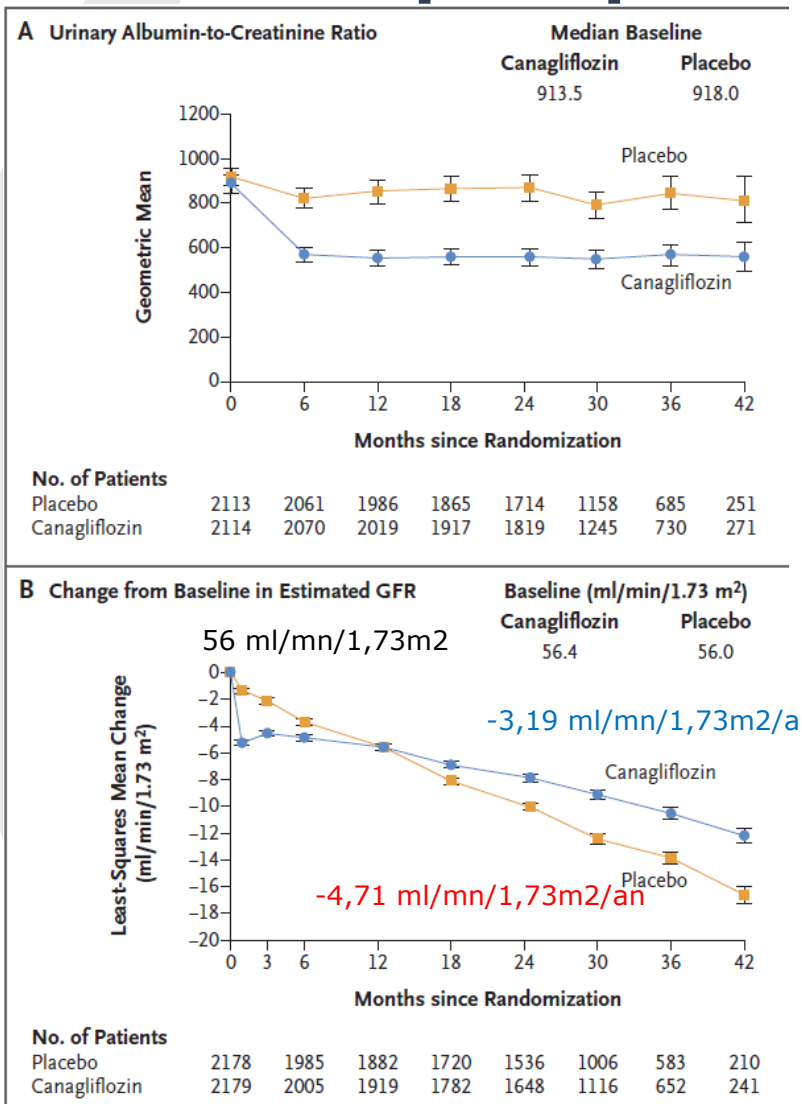


Figure 3. Effects on Albuminuria and Estimated GFR.

tary Appendix). On average, levels were lower in the canagliflozin group for systolic blood pressure (by 3.30 mm Hg; 95% CI, 2.73 to 3.87), diastolic blood pressure (by 0.95 mm Hg; 95% CI, 0.61 to 1.28), and body weight (by 0.80 kg;

?

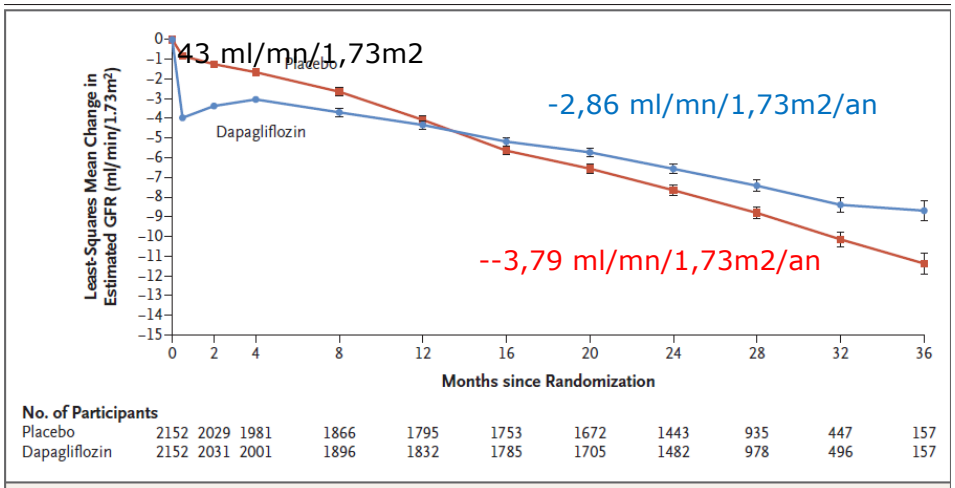


Figure 3. Change from Baseline in Estimated GFR.

L'heure de la prise

- Une question qui pourrait paraitre futile.
- Hygia Chronotherapy trial: >19000 patients espagnols, 60 ans, gros, 30% MRC, 20% DNID. TAS: 149 mm Hg 50% non dippers
- Intervention randomisée, tous les médicaments anti hypertenseurs le matin ou le soir.

Estimated glomerular filtration rate	79.0 ± 24.7	78.6 ± 25.5	79.3 ± 24.0	0.160
Albumin/creatinine (Cr) ratio, mg/g_{Cr}, median (interquartile range)	6.0 (3.0–16.6)	6.0 (3.0–15.9)	6.0 (3.0–17.1)	0.272

6,3 ans

Estimated glomerular filtration rate	75.7 ± 26.9	79.3 ± 23.5	<0.001
Albumin/creatinine (Cr) ratio, mg/g_{Cr}, median (interquartile range)	7.0 (3.7–20.0)	6.5 (3.6–18.0)	0.030
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
Non-dipper, %	50.3	37.5	<0.001

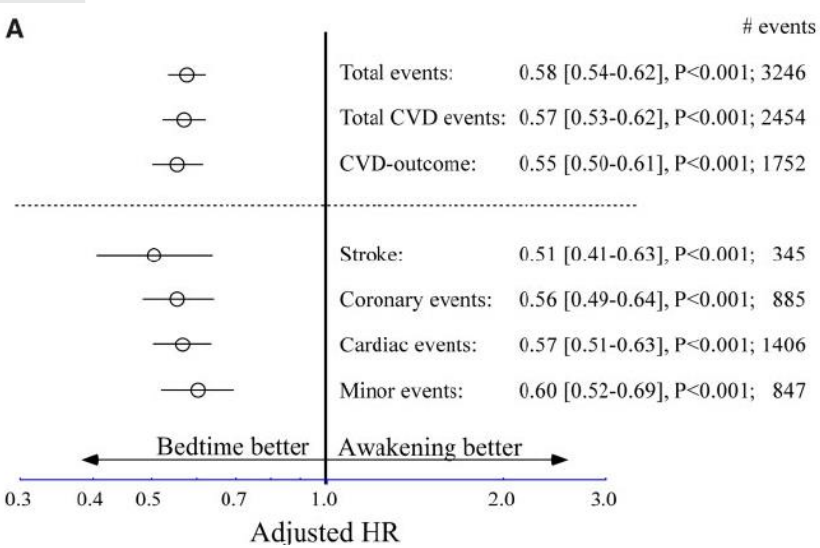
European Heart Journal (2019) **0**, 1–12
doi:10.1093/eurheartj/ehz754

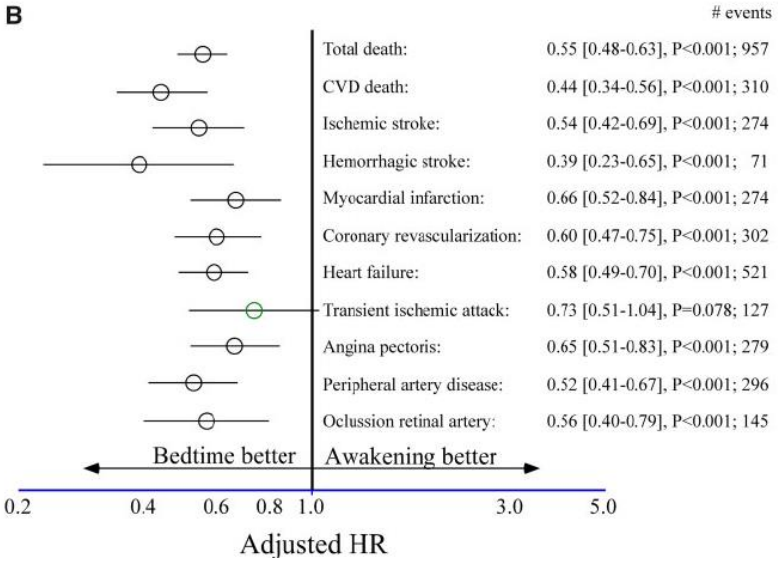
L'heure de la prise

- Une limite en fin d'étude

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

- Résultats impressionnants





En pratique

- L'HTA est un vrai problème de néphrologue
- L'HTA a un impact sur la survie des patients avec une MRC (maladie cardiovasculaire)
- La MRC entraine une HTA, l'inverse n'est pas sur
- Le traitement de première ligne est IEC ou Sartans+thiazidique ou CCB en une prise au coucher et le régime sans alcool.
- L'objectif<140 certainement <130 dans certains cas
- En cas de résistance, pensez à la spironolactone
- Encore beaucoup de choses à dire sur le sujet