Hypertension in patients on chronic dialysis

Csaba Ambrus

Szent Imre Teaching Hospital, Div. of Nephrology-Hypertension

Semmelweis University, Div.Sect. of Geriatric Medicine

B.Braun Avitum Hungary, Budapest

Global prevalence of dialysis patients

3 000 000 patients on dialysis

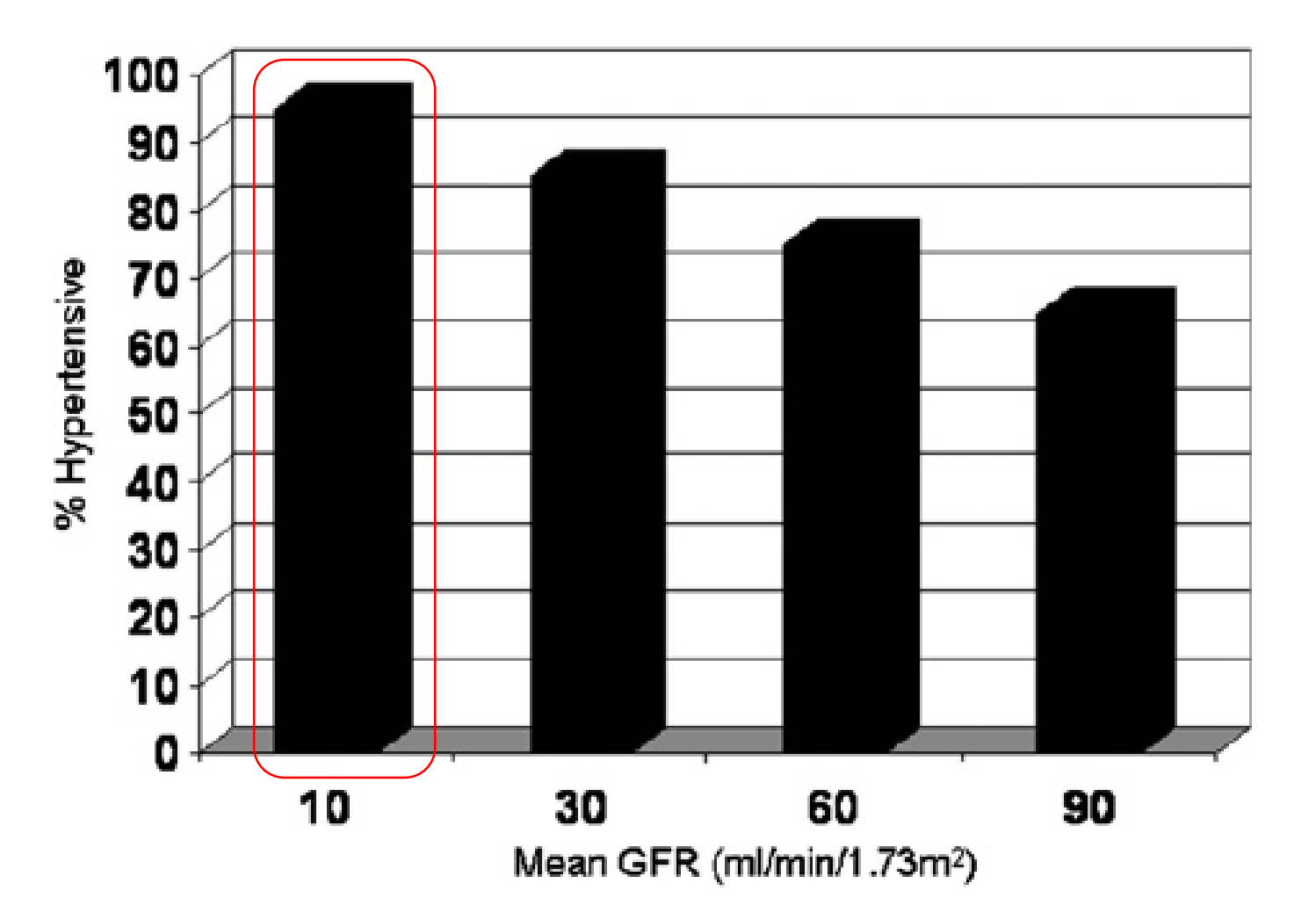
89%

hemodialysis (HD)

11%

peritoneal dialysis (PD)

Prevalence of hypertension in dialysis patients



MDRD, Am J Kidney Dis 1996;28:811–21

Prevalence of hypertension in dialysis patients

Reference	Year	*N*	Definition of hypertension	Prevalence of hypertension (%)	BP treatment among hypertensive patients (%)	BP control among hypertensive patients (%)
Salem [55]	1995	649	Prehemodialysis MAP ≥ 114 mmHg or use of antihypertensive agents	71.9	81.5	48.6
Rahman *et al.* [60]	1999	489	Prehemodialysis SBP ≥ 140 mmHg and/or DBP ≥ 90 mm	87.7	93.2	71.1
Agarwal *et al.* [1]	2003	2535	1-week average prehemodialysis SBP > 150 mmHg and/or DBP > 85 mmHg, or use of antihypertensive agents	85.8	88.4	30.3
Agarwal [56]	2011	369	44-h interdialytic ambulatory SBP ≥ 135 mmHg and/or DBP ≥ 85 mmHg or use of antihypertensive medications	82	89	38
Cocchi	1999	444	24h ABPM: SBP>140, DBP>90, or antihypertensive medication	88.1	81.5	22.7
Inal	2012	37	office BP > 140/90mmHg	73	-	37

The most common cause, consequence, co-morbidity: *70-80-90% ?*

Sarafidis et al, J Hypertens. 2017;35(4):657-676.
Inal et al, Adv Perit Dial. 2012;28:10-15.
Cocchi et al, Nephrol Dial Transplant 1999;14:1536–40.

Prevalence of hypertension in dialysis patients

Reference	Year	*N*	Definition of hypertension	Prevalence of hypertension (%)	BP treatment among hypertensive patients (%)	BP control among hypertensive patients (%)
Salem [55]	1995	649	Prehemodialysis MAP ≥ 114 mmHg or use of antihypertensive agents	71.9	81.5	48.6
Rahman *et al.* [60]	1999	489	Prehemodialysis SBP ≥ 140 mmHg and/or DBP ≥ 90 mm	87.7	93.2	71.1
Agarwal *et al.* [1]	2003	2535	1-week average prehemodialysis SBP > 150 mmHg and/or DBP > 85 mmHg or use of antihypertensive agents	85.8	88.4	30.3
Agarwal [56]	2011	369	44-h interdialytic ambulatory SBP ≥ 135 mmHg and/or DBP ≥ 85 mmHg or use of antihypertensive medications	82	89	38
Cocchi	1999	444	24h ABPM, SBP>140, DBP>90, or antihypertensive medication	88.1	81.5	22.7
Inal	2012	37	office BP > 140/90mmHg	73	-	37

it depends on how we define hypertension

High prevalence of hypertension and

Poor BP control among both HD and PD patients !

Sarafidis et al, J Hypertens. 2017;35(4):657-676.
Inal et al, Adv Perit Dial. 2012;28:10-15.
Cocchi et al, Nephrol Dial Transplant 1999;14:1536–40.

Prevalence of hypertension in dialysis patients

Reference	Year	*N*	Definition of hypertension	Prevalence of hypertension (%)		BP treatment among hypertensive patients (%)		BP control among hypertensive patients (%)	
Salem [55]	1995	649	Prehemodialysis MAP ≥ 114 mmHg or use of antihypertensive agents	71.9	**81%**	81.5	**89%**	48.6	**65%**
Rahman *et al.* [60]	1999	489	Prehemodialysis SBP ≥ 140 mmHg and/or DBP ≥ 90 mm	87.7	**76%**	93.2	**75%**	71.1	**62%**
Agarwal *et al.* [1]	2003	2535	1-week average prehemodialysis SBP > 150 mmHg and/or DBP > 85 mmHg, or use of antihypertensive agents	85.8	**88%**	88.4	**82%**	30.3	**58%**
Agarwal [56]	2011	369	44-h interdialytic ambulatory SBP ≥ 135 mmHg and/or DBP ≥ 85 mmHg or use of antihypertensive medications	82	**92%**	89	**75%**	38	**62%**
Cocchi	1999	444	24h ABPM: SBP>140, DBP>90, or antihypertensive medication	88.1		81.5		22.7	
Inal	2012	37	office BP > 140/90mmHg	73		-		37	

High prevalence of hypertension and

Poor BP control among both HD and PD patients !

Sarafidis et al, J Hypertens. 2017;35(4):657-676.

Inal et al, Adv Perit Dial. 2012;28:10-15.

Cocchi et al, Nephrol Dial Transplant 1999;14:1536–40.

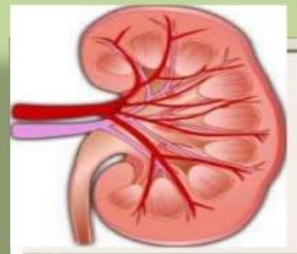
Hypertension guidelines in kidney disease

Therapeutic strategies for treatment of hypertension in 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

©ESC/ESH 2018

Blood pressure targets recommendations in CKD



	Blood pressure target in CKD without proteinuria*	Blood pressure target in CKD with proteinuria
USA JNC8[91]	<140/<90 mmHg	<140/<90 mmHg
KDIGO[76]	<140/<90 mmHg	<130/<80 mmHg
NICE[80]	<140/<90 mmHg	<130/<80 mmHg
CHEP[78]	<140/<90 mmHg	<140/<90 mmHg
ESC/ESH[79]	<140 mmHg	<130 mmHg
ASH/ISH[123]	<140/<90 mmHg	<140/<90 mmHg§
ISHIB[124]	<130/<80 mmHg	<130/<80 mmHg

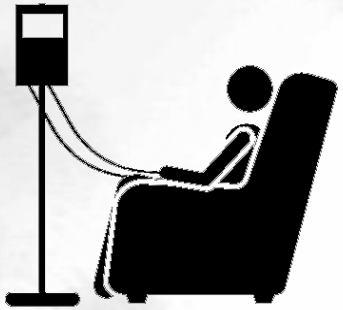
Hypertension guidelines in kidney disease …

Therapeutic strategies for treatment of hypertension in 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

©ESC/ESH 2018

and in
Hemodialysis &
Peritoneal dialysis ?

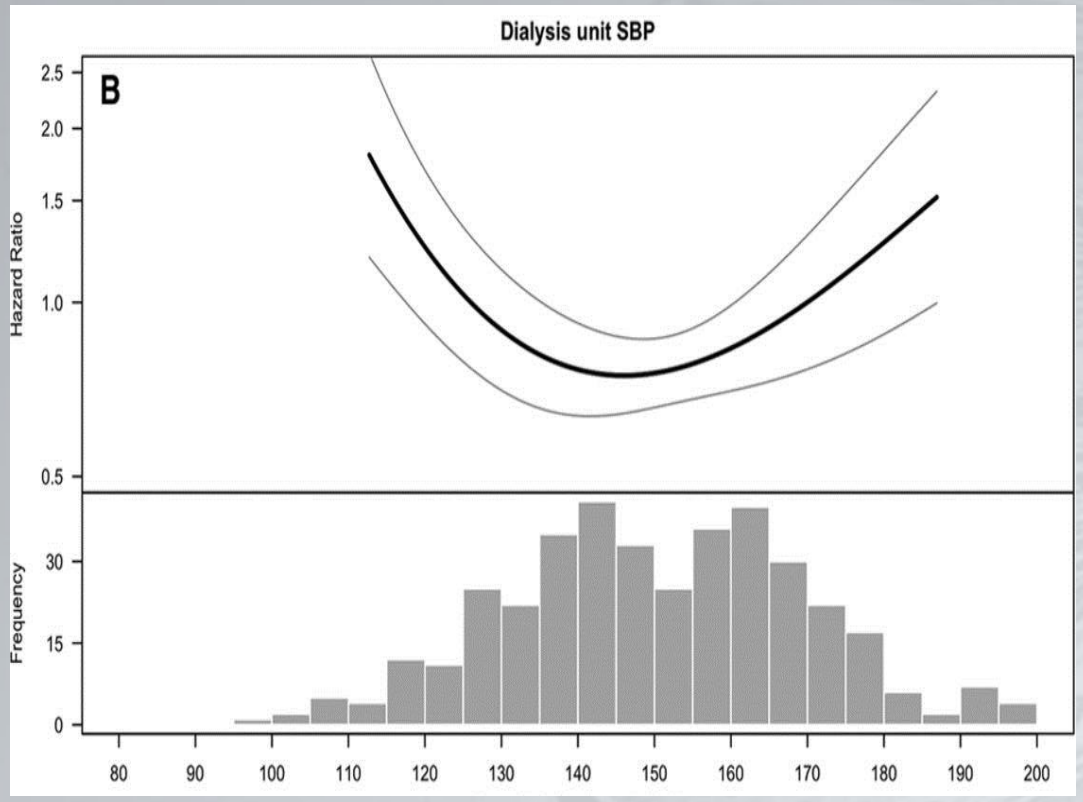


Blood pressure and mortality in dialysis

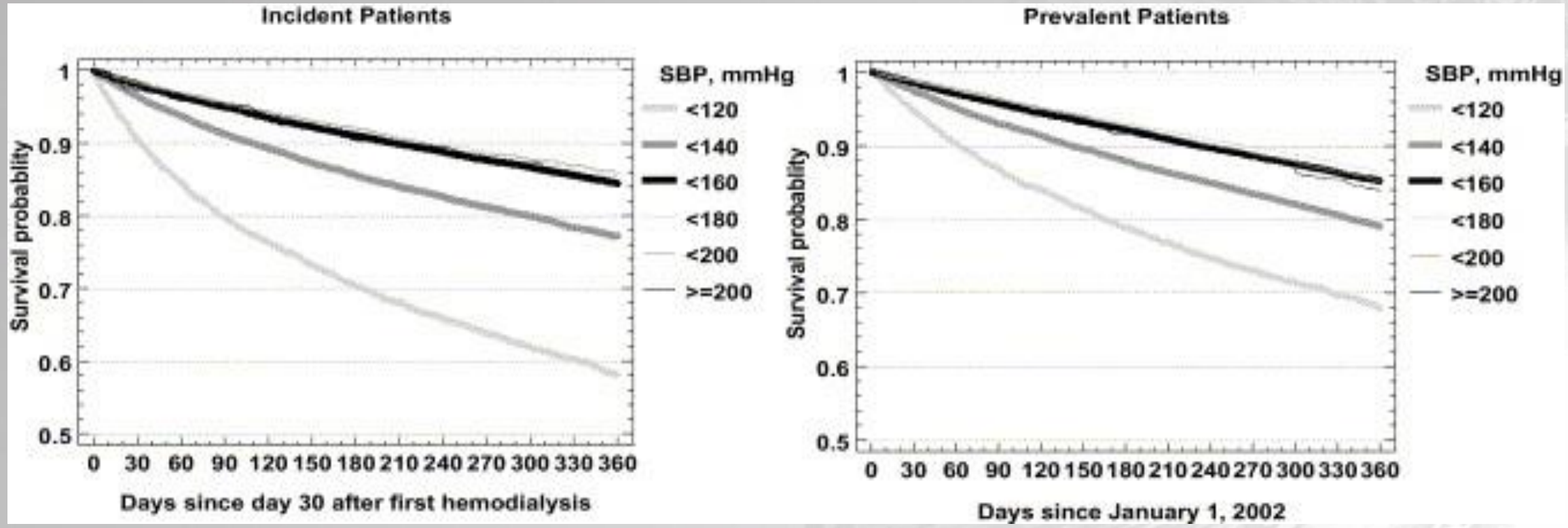
- Is “esreveR” epidemiology a unique feature in dialysis patients ?

  paradoxical relationship between traditional risk factors and mortality

  - blood pressure
  - body weight
  - cholesterol
  - creatinine
  - homocystein
  - osteoprotegerin



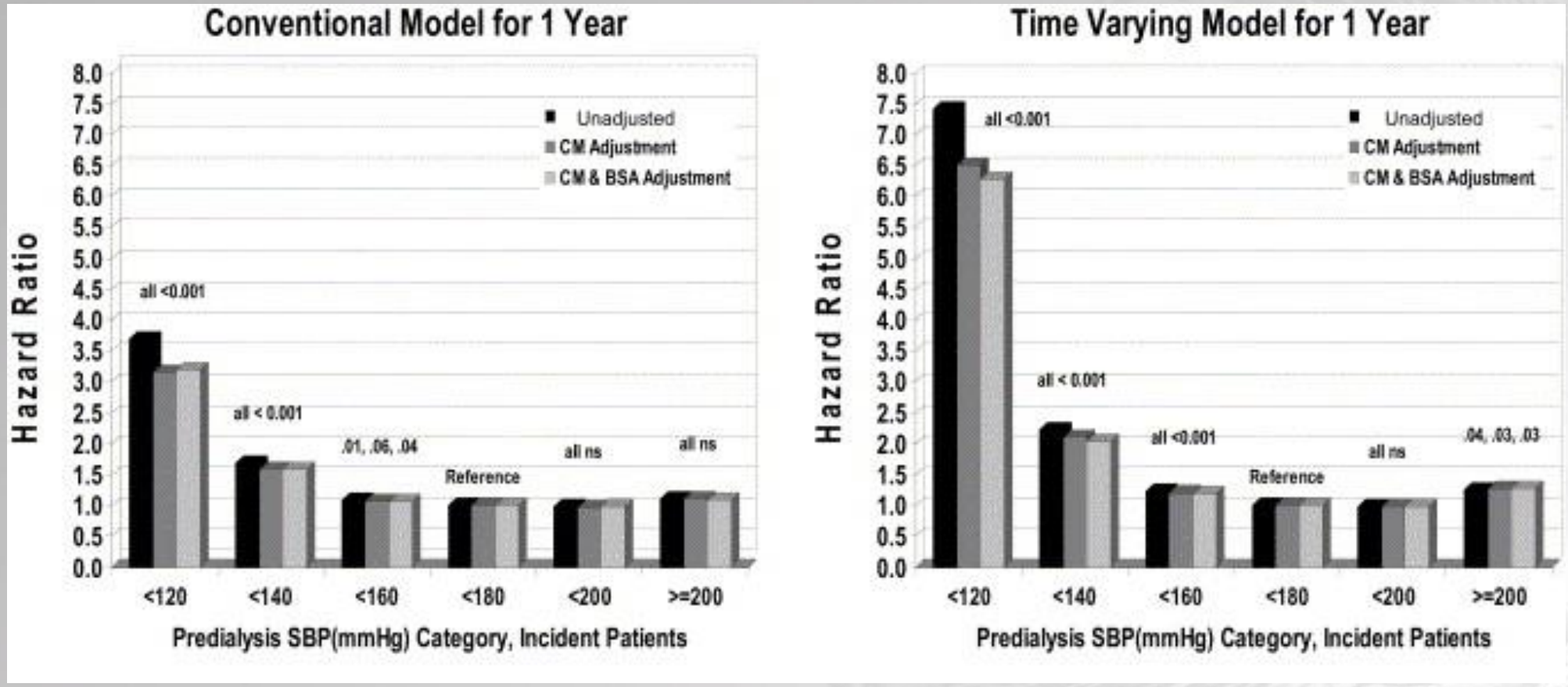
Blood pressure and mortality in dialysis



65338 incident and 69590 prevalent HD patients, 1 year survival

Zhensheng et al, AJKD 2006; 48:606-615

Blood pressure and mortality in dialysis

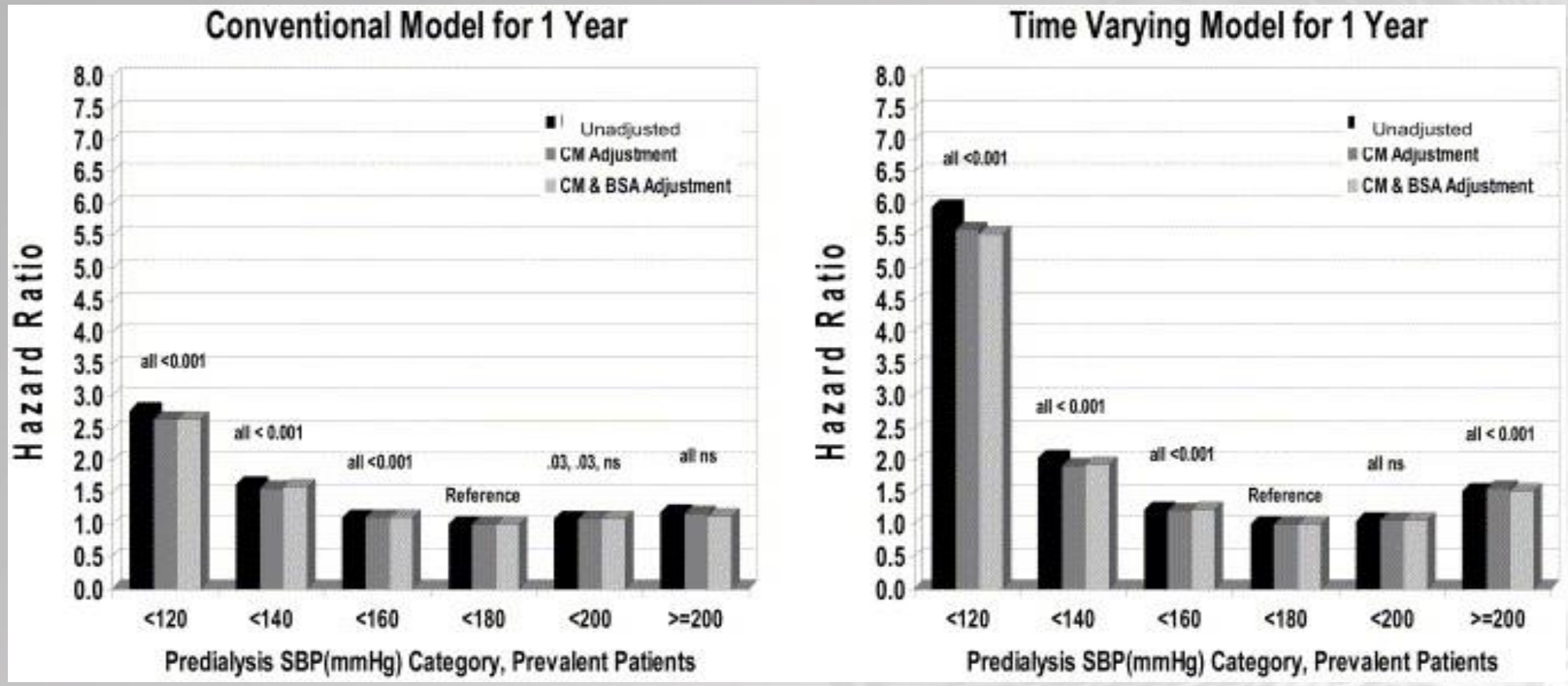


65338 incident and 69590 prevalent HD patients, 3 year survival

Incident sample, CV events: 59.2%

Zhensheng et al, AJKD 2006; 48:606-615

Blood pressure and mortality in dialysis

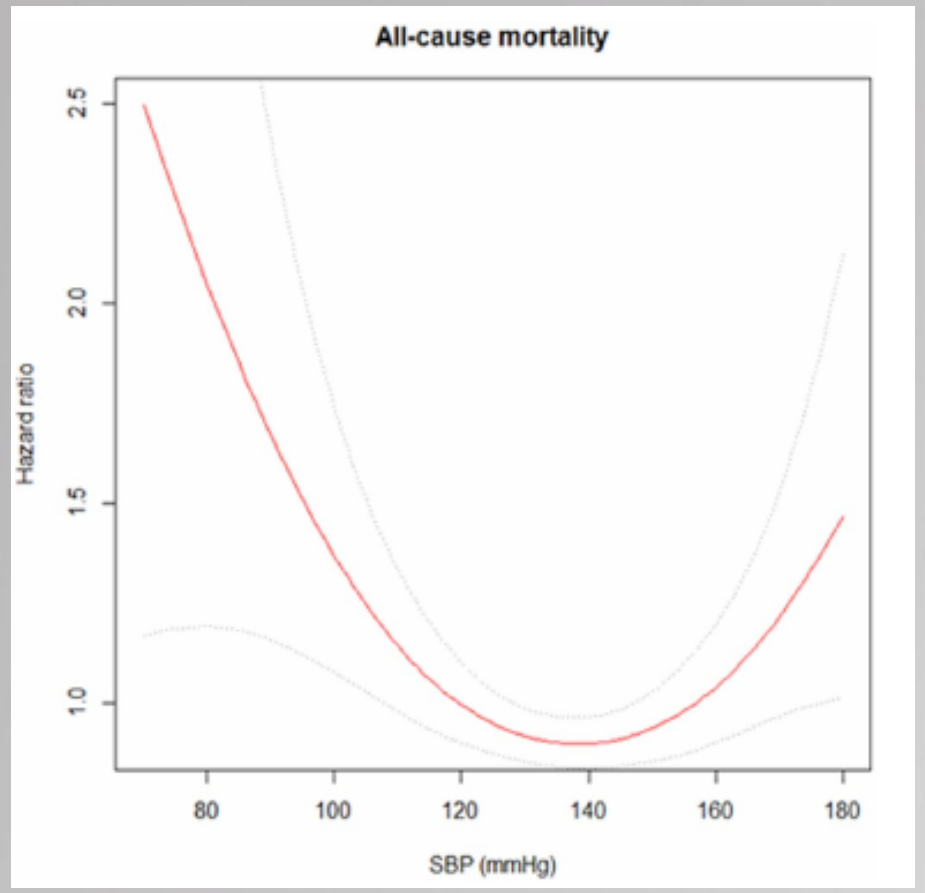


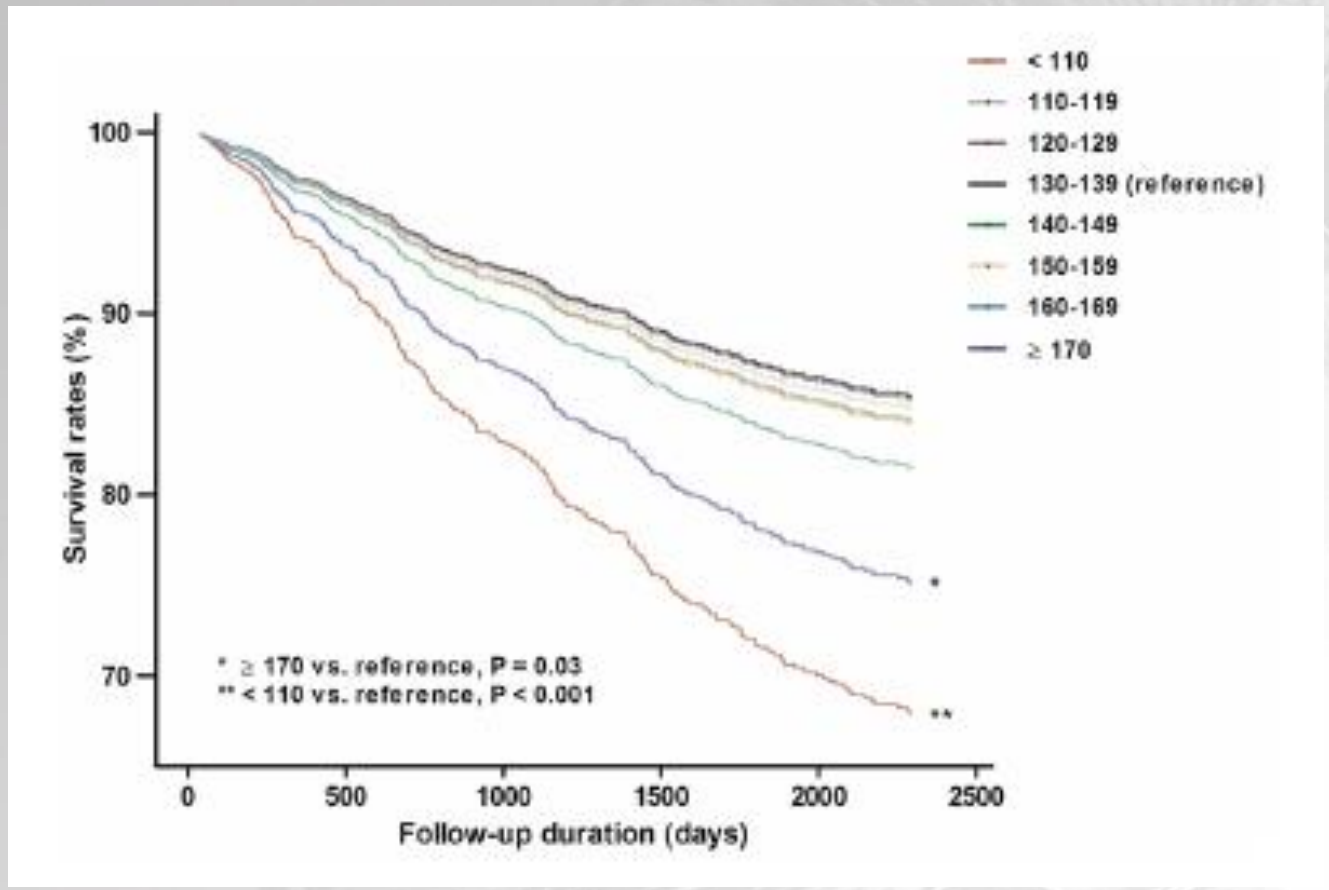
65338 incident and 69590 prevalent HD patients, 3 year survival

Prevalent sample, CV events: 60.2%

Zhensheng et al, AJKD 2006; 48:606-615

Blood pressure and mortality in dialysis





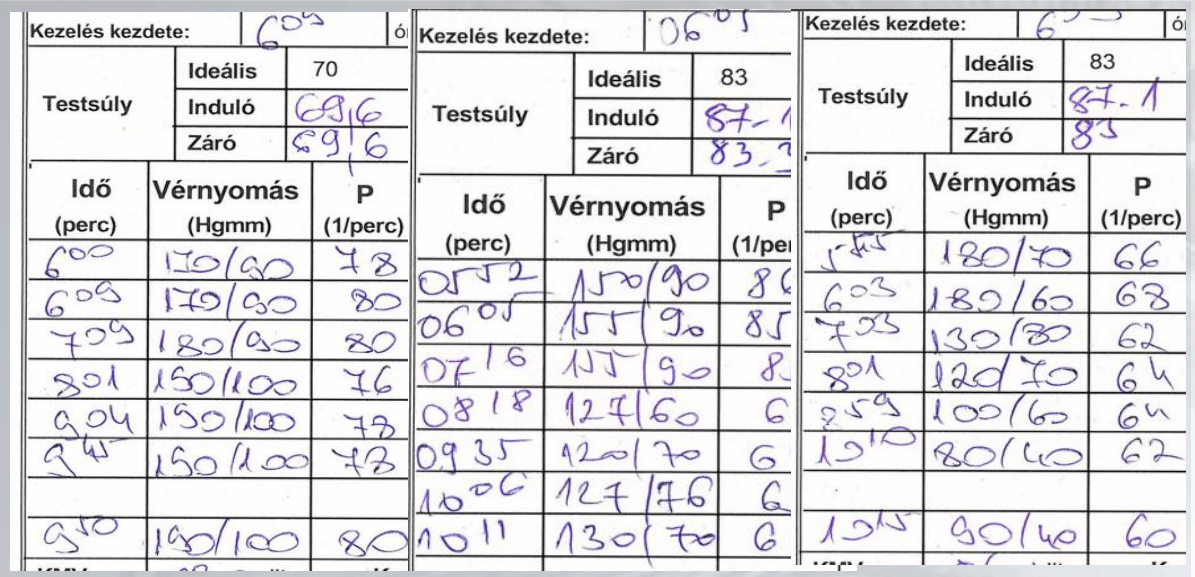
2299 prevalent HD & PD patients, 4.5 year follow-up

Jhee et al, Sci Rep 2018; 8:14123

How should we define hypertension on dialysis?

Diagnosis based on:

- pre-dialysis blood pressure
- post-dialysis blood pressure



Kezelés kezdete:		
Testsúly	Ideális	70
	Induló	69,6
	Záró	69,6

Idő (perc)	Vérnyomás (Hgmm)	P (1/perc)
600	130/90	78
609	170/90	80
709	180/90	80
801	150/100	76
904	150/100	78
945	150/100	78
950	150/100	80

Kezelés kezdete:		
Testsúly	Ideális	83
	Induló	87,1
	Záró	83,7

Idő (perc)	Vérnyomás (Hgmm)	P (1/per
0552	150/90	8
0605	155/90	85
0716	155/90	8
0818	127/60	6
0935	120/70	6
1006	127/76	6
1011	130/70	6

Kezelés kezdete:		
Testsúly	Ideális	83
	Induló	87,1
	Záró	83

Idő (perc)	Vérnyomás (Hgmm)	P (1/perc)
555	180/70	66
603	180/60	68
703	130/80	62
801	120/70	64
859	100/60	64
1510	80/40	62
1515	90/40	60

- myriad of measurements available
- convenient and tempting method
- but only useful to ensure hemodynamic stability during HD

Not suitable for diagnosing hypertension !

Problems with peri-dialysis BP

Peri-dialysis BP is not suitable for diagnosing hypertension !

Many factors affecting pre-dialysis BP

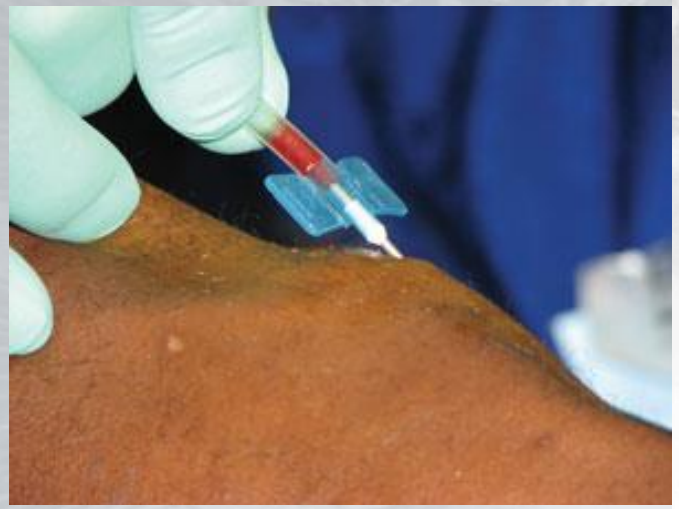
- impatient patient
  (early start, early escape from unit)
- needle-effect
- white-coat effect (30% of dialysis patient!)
- pre-dialysis BP highly depends on volume status
  (interdialysis weight gain)

Post-dialysis BP depends on ultrafiltration rate, ...

Technique not standardized

Problems with peri-dialysis BP

Peri-dialysis BP is not suitable for diagnosing hypertension !



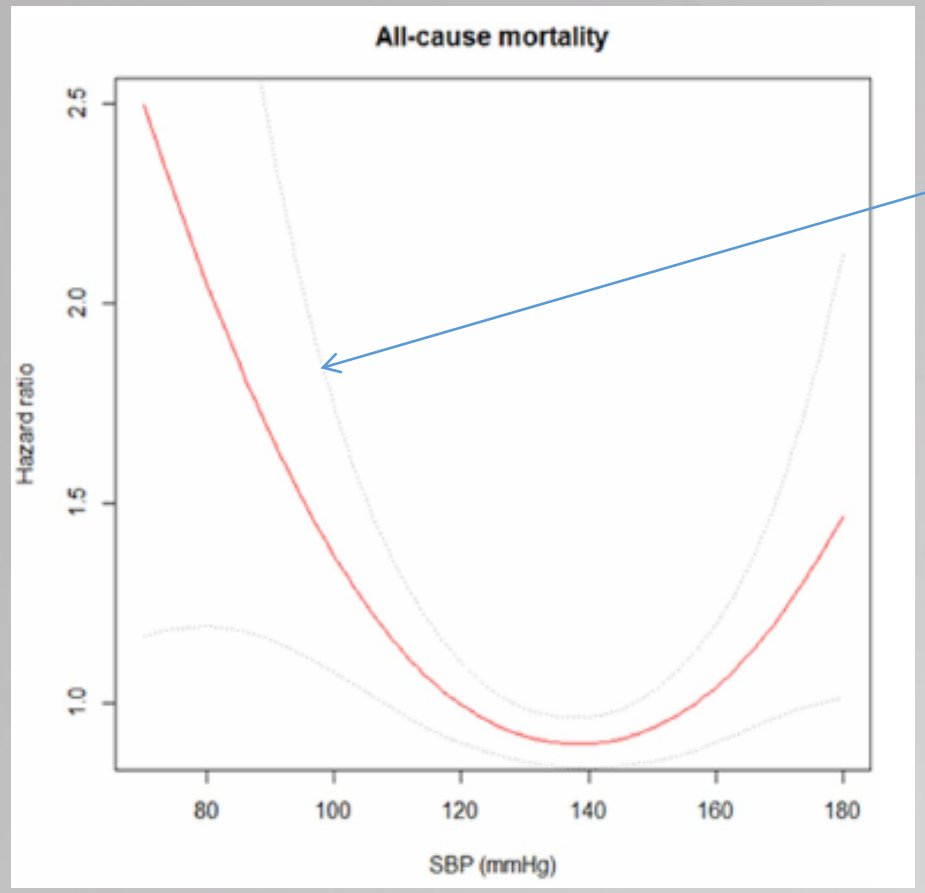
Many factors affecting pre-dialysis BP

- impatient patient
  (early start, early escape from unit)
- needle-effect
- white-coat effect (30% of dialysis patient!)
- pre-dialysis BP highly depends on volume status
  (interdialysis weight gain)

Post-dialysis BP depends on ultrafiltration rate, ...

Technique not standardized

Problems with peri-dialysis BP

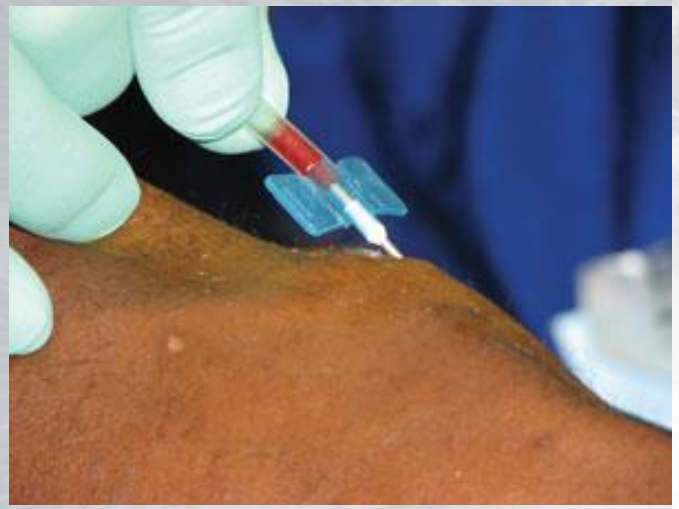


Failure of normal stress response?

Jhee et al, Sci Rep 2018; 8:14123

Problems with peri-dialysis BP

Peri-dialysis BP is not suitable for diagnosing hypertension !



Many factors affecting pre-dialysis BP

- impatient patient
  (early start, early escape from unit)
- needle-effect
- white-coat effect (30% of dialysis patient!)
- pre-dialysis BP highly depends on volume status
  (interdialysis weight gain)

Post-dialysis BP depends on ultrafiltration rate, ...

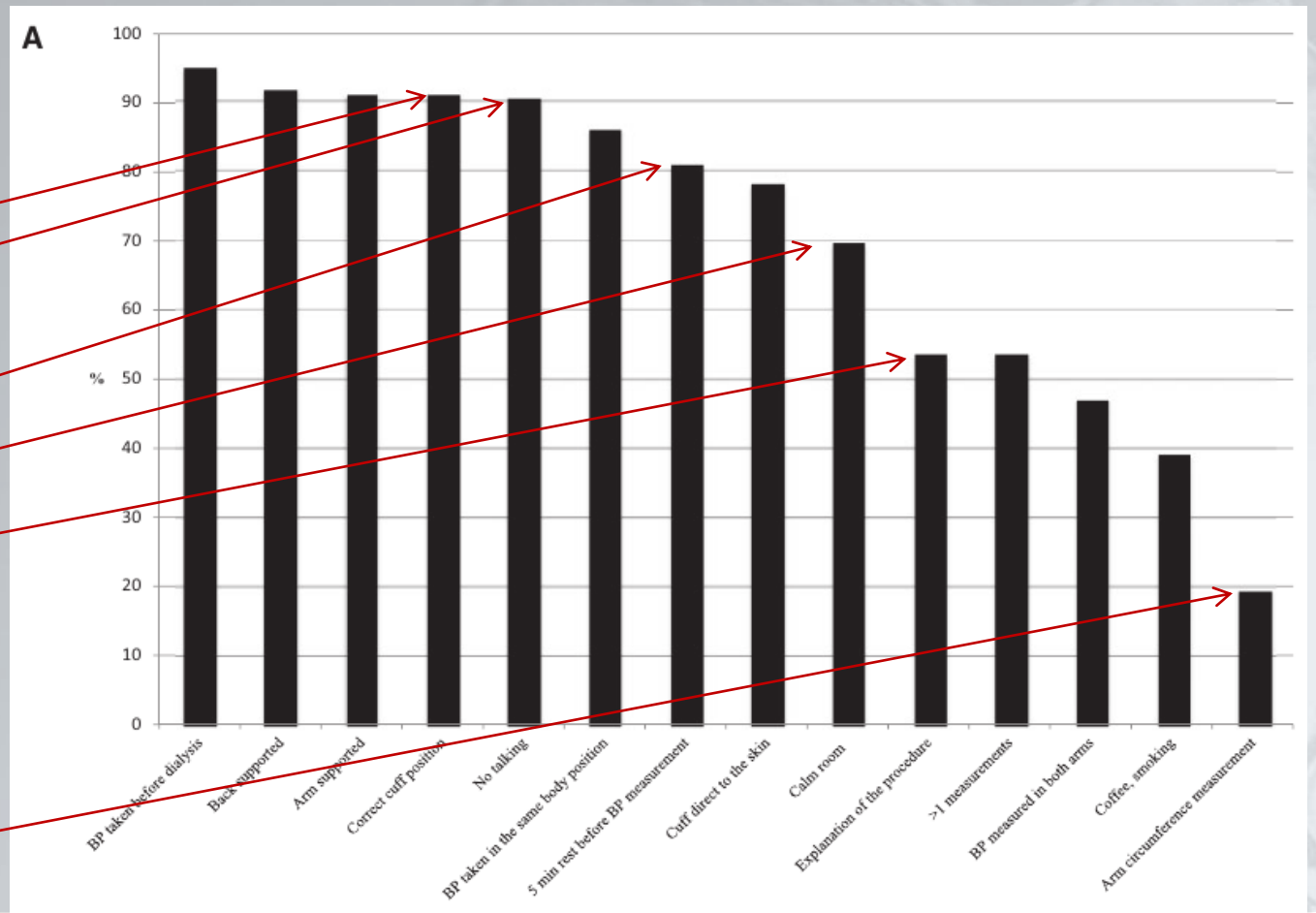
Technique not standardized

Problems with peri-dialysis BP

BP measurement technique not standardized

multi-center survey - proportion of physicians adhering to recommendations

BP taken before dialysis
back supported
arm supported
correct cuff position
no talking
same body position
taken after 5 min rest
cuff direct to skin
calm room
explanation of procedure
>1 measurements
both arms
arm circumferenc measurement



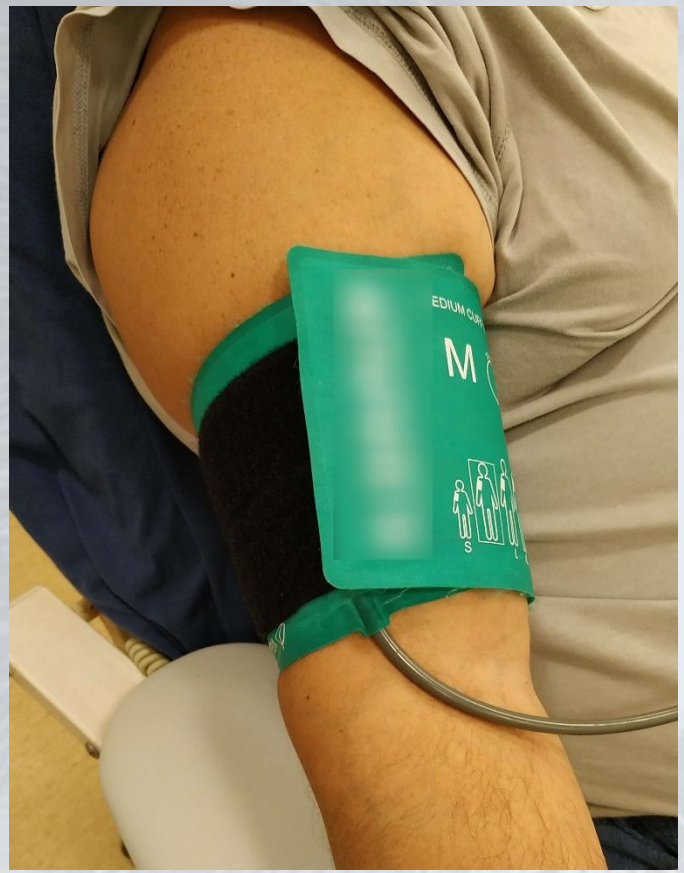
Pappaccogli et al, Nephrol Dial Transplant (2019) 1–4

Problems with peri-dialysis BP

BP measurement technique not standardized

multi-center, cross sectional survey - proportion of physicians adhering to recommendations

BP taken before dialysis
back supported
arm supported
correct cuff position
no talking
same body position
taken after 5 min rest
cuff direct to skin
calm room
explanation of procedure
>1 measurements
both arms
arm circumferenc measurement



Hypertension and mortality in patients on PD

- NECOSAD study, 118 incident PD patients

  +42% relative risk
  for each 10mmHg SBP

Table 5. Multivariate Cox proportional hazards model for patient survival using urinary and dialysate creatinine appearance

Factor	Relative risk	95% Confidence interval
Age *1 year*	1.05	1.01–1.09
Systolic blood pressure *10 mm Hg*[a]	1.42	1.17–1.73
Urinary creatinine appearance *1 mmol/week/1.73 m²*[b]	0.95	0.92–0.98
Dialysate creatinine appearance *1 mmol/week/1.73 m²*[b]	0.93	0.89–0.98

[a] $P < 0.001$; [b] $P < 0.01$

- England and Wales, 3086 incident PD patients

  association btw BP and survival varies over time:

  •in 1st year: higher SBP, DBP - lower mortality (= contraselection of sic patients)

  •>5 year survivors: higher SBP - higher mortality

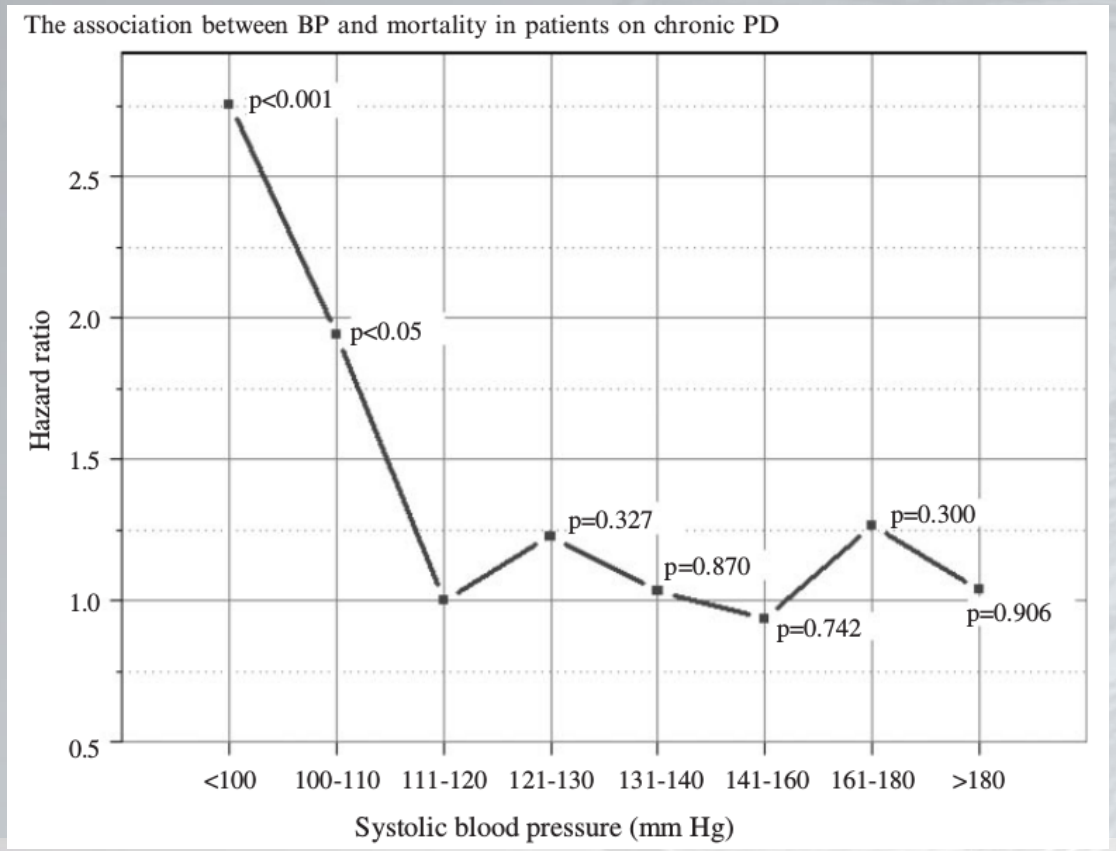
Jager et al, Kidney Int. 1999;55(4):1476-1485.
Udayaraj et al, American Journal of Kidney Diseases 2009; 53(1):70–78

Hypertension and mortality in patients on PD

- USRDS, 1053 incident PD patients

Higher CV & all-cause mortality if SBP < 110mmHg

only in patients with heart failure or diabetes or antihypertensive medication



*

Goldfarb-Rumyantzev et al, Nephrol Dial Transplant. 2005;20(8):1693-1701.

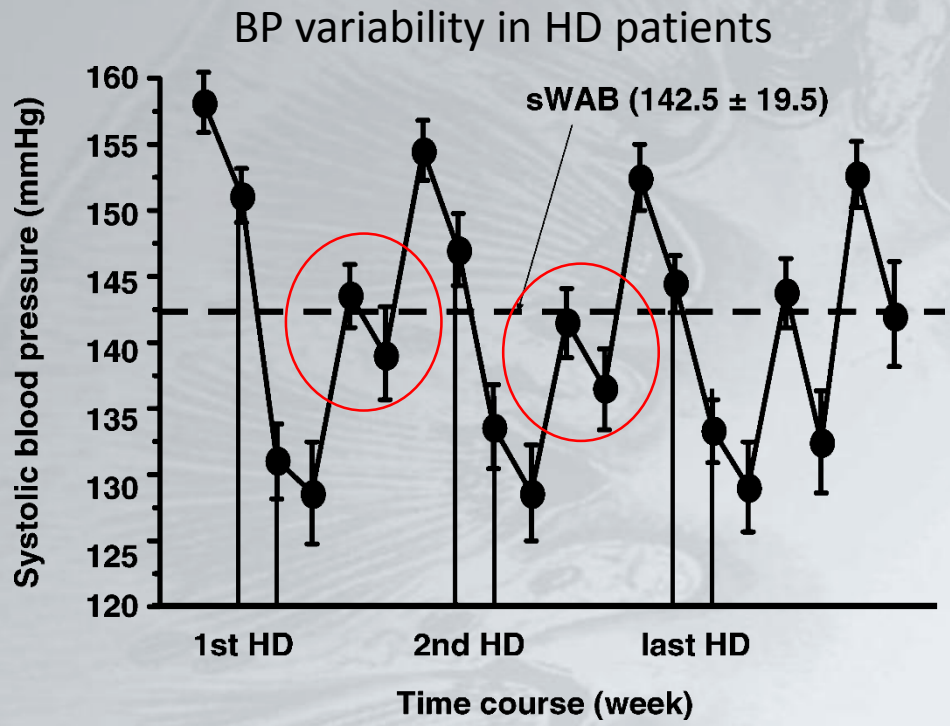
What is the useful definition for hypertension ?

Diagnosis based on:

- ~~pre-dialysis blood pressure~~
- ~~post-dialysis blood pressure~~

- interdialytic BP outside dialysis unit
  - office BP on non-dialysis days
  - home BP measurements
  - 24/44 hour ABPM

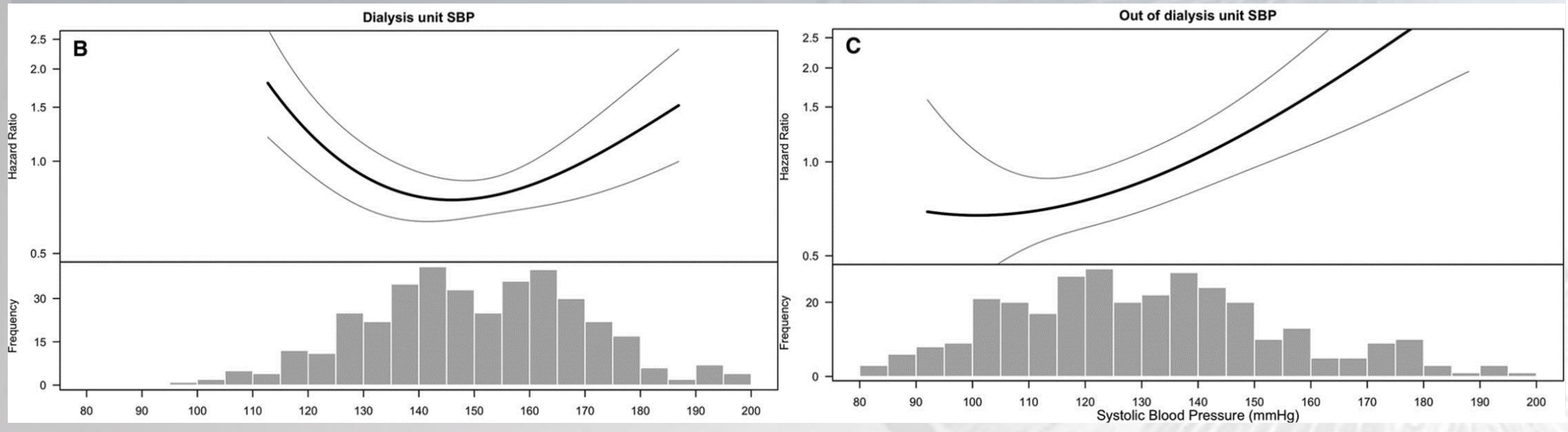
- Home or office BP measurements for PD patients



Miskulin et al, Semin Dial. March 2017.

Hypertension and mortality: peri-dial vs H/ABPM

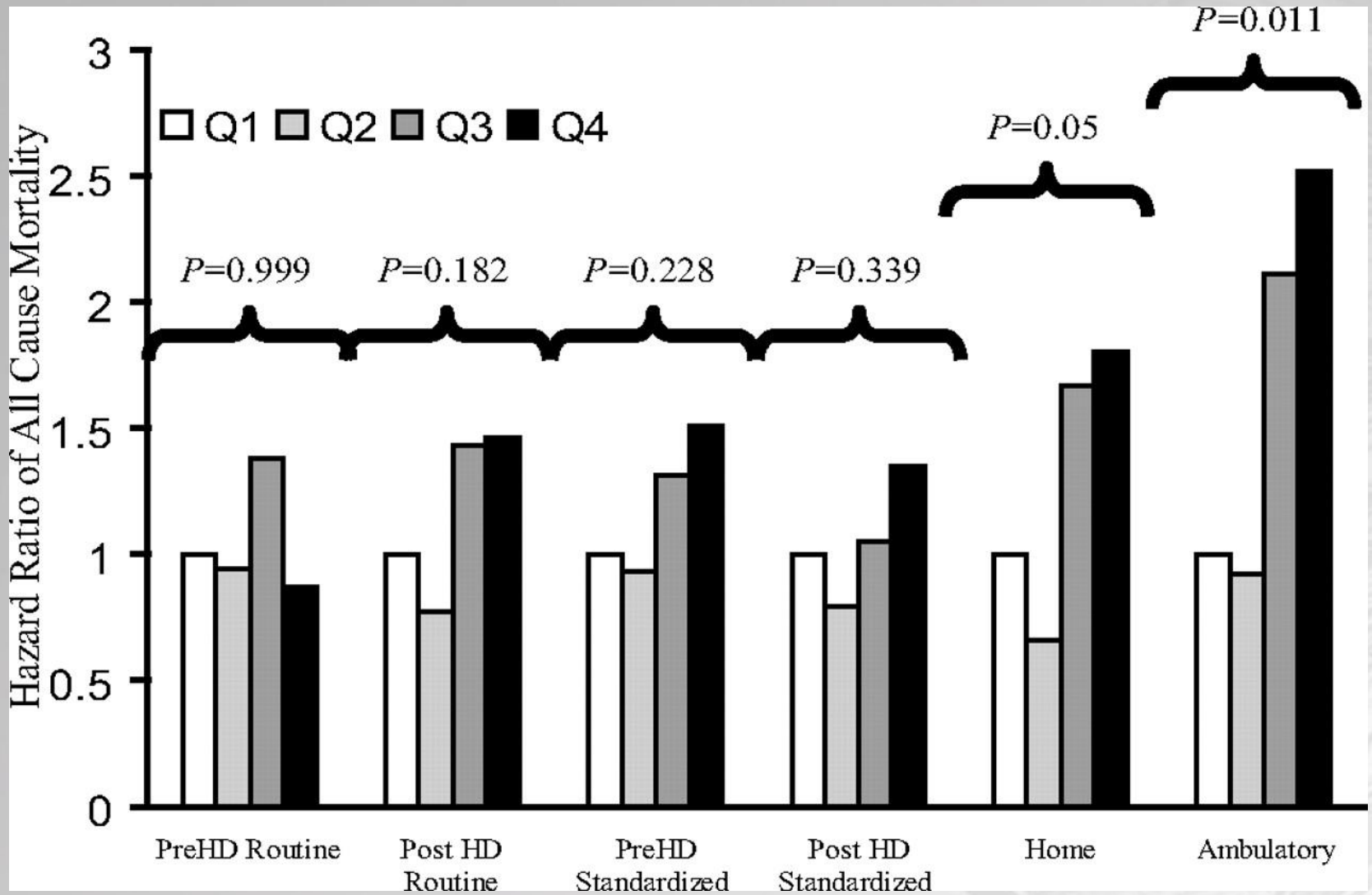
- Pre-dialysis BP and mortality:
  - U-shaped association - a "reverse epidemiology"?
    higher mortality with SBP < 130 or SBP > 160 mmHg
  - lack on normal response to stress @ dialysis start (background cardiovascular disease?)
  - associations not adjusted for cardiac function, co-morbidities, medication
- Home BP or ABPM
  - linear associations, more reliable and reproducible



Nisha Bansal et al. Hypertension. 2015;65:93-100

Hypertension and mortality: peri-dial vs H/ABPM

No associations when using pre-, or post-dialysis measurements.



Home BP

Q1: < 125.7

Q2: 125.7 - 143.6

Q3: 143.6 - 157.9

Q4: > 157.9

ABPM

Q1: < 113.5

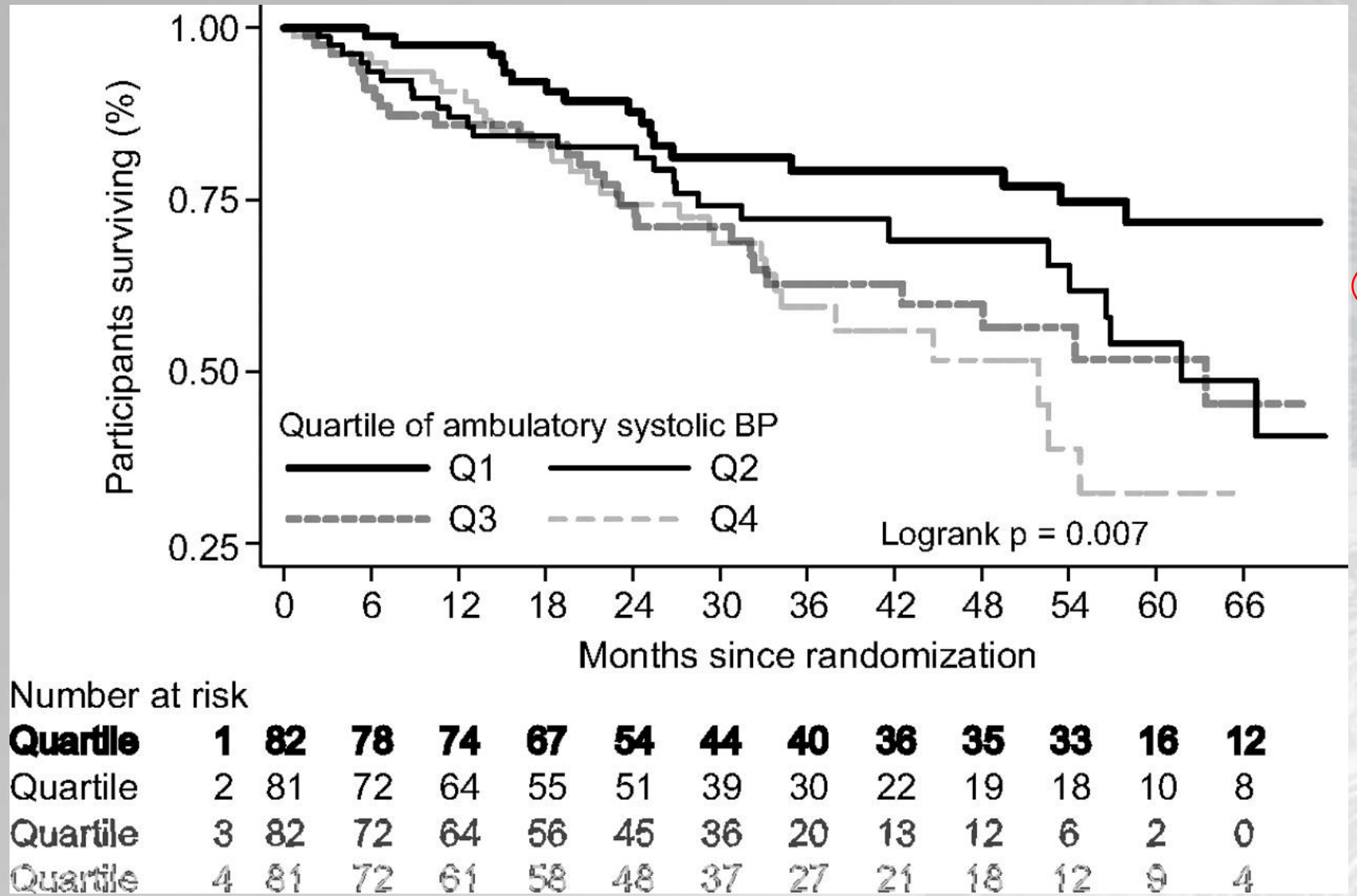
Q2: 113.5 - 125

Q3: 125 - 145

Q4: > 145

Pooneh Alborzi et al. CJASN 2007;2:1228-1234

Hypertension and mortality: ABPM



ABPM SBP

Q1: < 119.2

Q2: 119.2 - 134.6

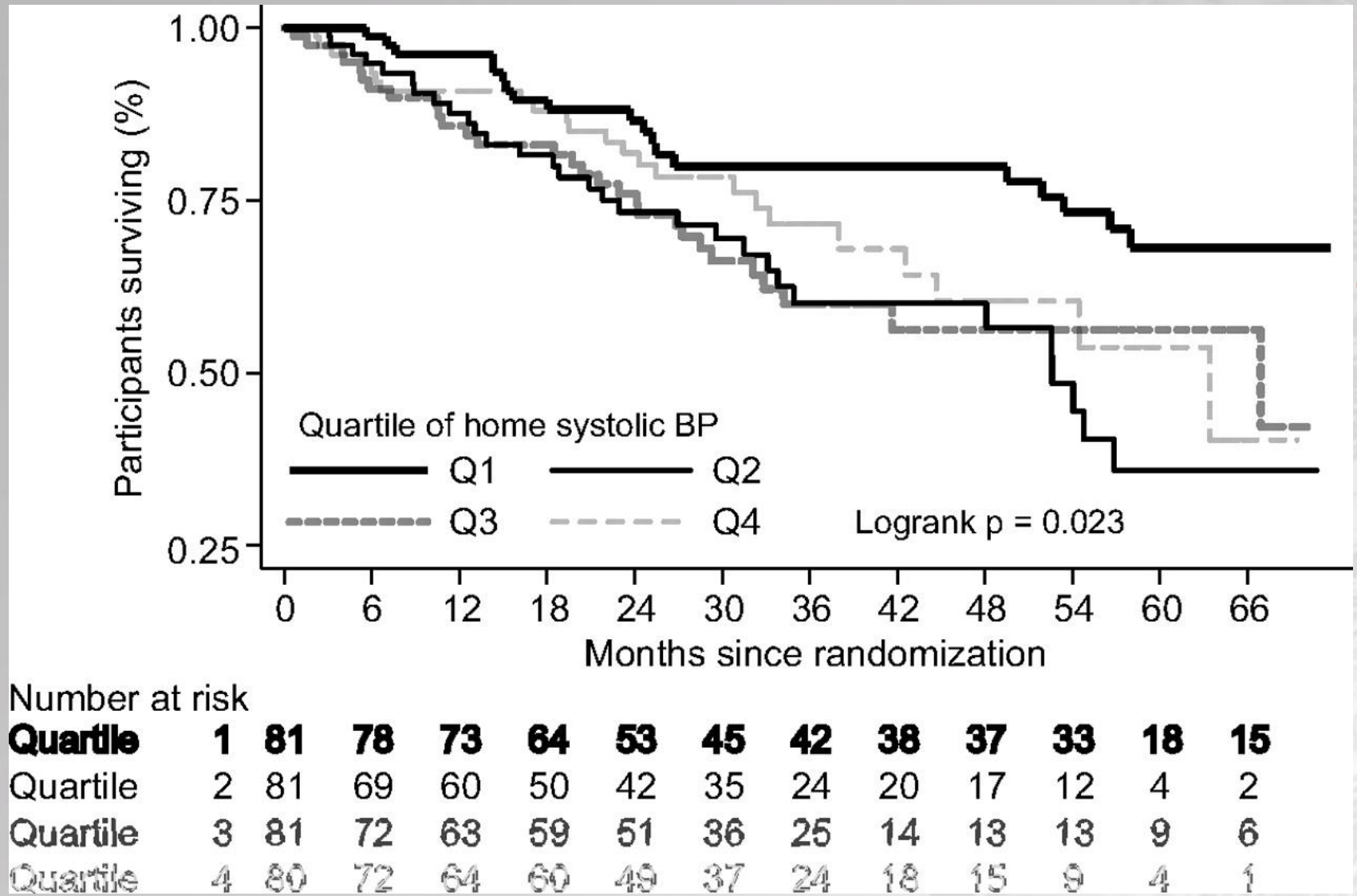
Q3: 134.6 - 146.1

Q4: > 146.1

*

Agarwal et al, Hypertension. 2010;55:762-768

Hypertension and mortality: HBPM



Number at risk

Quartile	**1**	**81**	**78**	**73**	**64**	**53**	**45**	**42**	**38**	**37**	**33**	**18**	**15**
Quartile	2	81	69	60	50	42	35	24	20	17	12	4	2
Quartile	3	81	72	63	59	51	36	25	14	13	13	9	6
Quartile	4	80	72	64	60	49	37	24	18	15	9	4	1

Home SBP

Q1: < 133

Q2: 133 - 149

Q3: 150 - 164

Q4: > 164

*

Agarwal et al, Hypertension. 2010;55:762-768

Diagnosis of hypertension in dialysis patients

EURECA Consensus 2017

- ABPM BP average ≥ 135/85 mmHg over 24 hours
  - HD: during mid-week, non-dialysis day
  - HD: exted to 44hours if feasible, covering whole interdialysis

- Home BP average ≥ 135/85 mmHg
  - HD: over 6 non-dialysis days, in the morning and evening
  - PD: over 7 consecutive days, in the morning and evening

- Office BP ≥ 140/90 mmHg
  - if home BP or ABPM not available
  - HD: on mid-week, non-dialysis day

quiet room, seated position, after 5 min rest, back & arm supported, 2 measurements 1-2 min apart

EURECA Consensus, J Hypertens. 2017;35(4):657-676.

BP outside the dialysis unit: ABPM

ABPM

- gold standard in the general population
- strong association with mortality and morbidity (both HD & PD)
- can detect masked or white-coat hypertension
- 44 hour interdialytic period covered
- additional night-time measurement

  non-dipping pattern is very common (50-60%) and linked to mortality

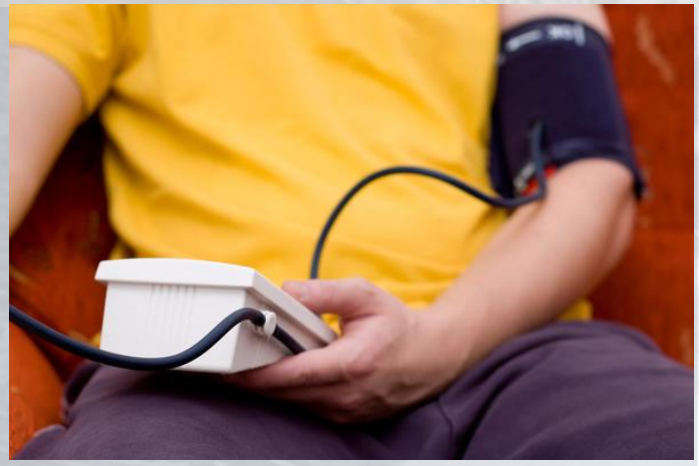
Feasibility?

- inconvenient for patients over 24-44 hours
- challenging in patients with (multiple, previous) AV fistulas
- limited availability, organizational barriers
- multiple assessment needed for follow-up of treatment

BP outside the dialysis unit: HBPM

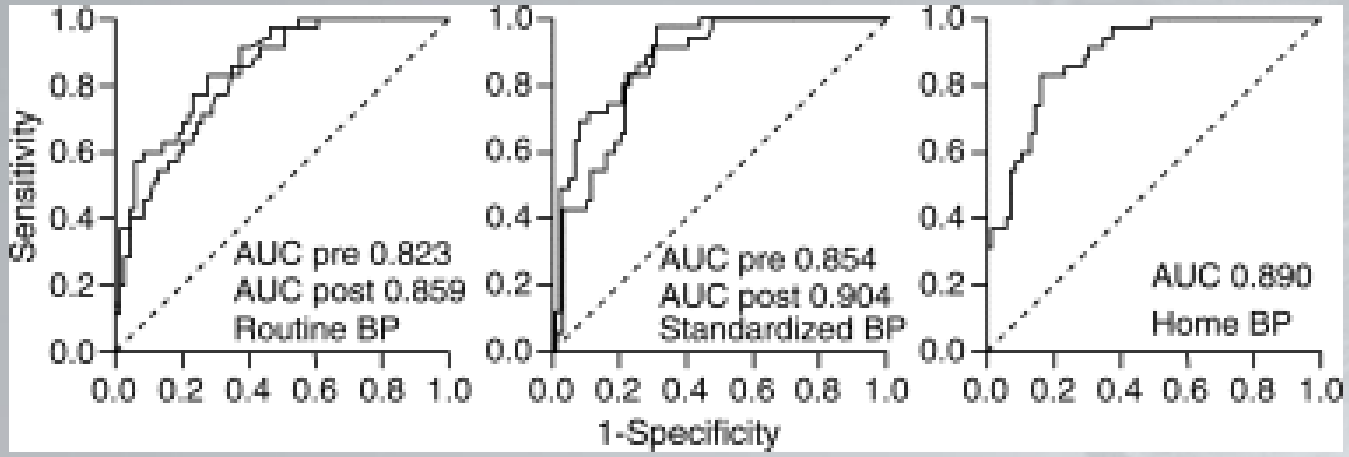
HBPM: home BP monitoring

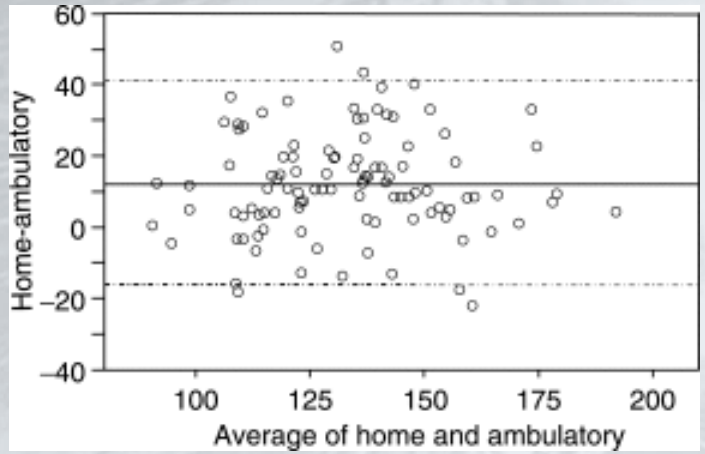
- measured on <u>non-dialysis days</u>



- good correlation to target-organ damage
- predictor of cardiovascular events and mortality

- best agreement with ABPM results (compared to peri-dial BP)



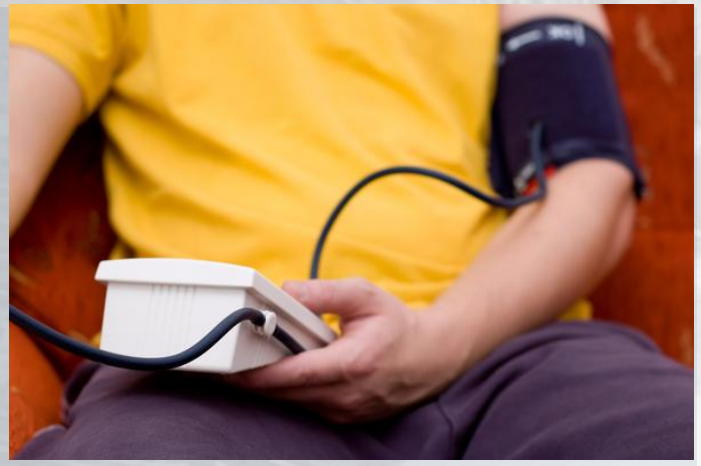


Kidney International 2006 69, 900-906

BP outside the dialysis unit: HBPM

HBPM: home BP monitoring

- measured on <u>non-dialysis days</u>



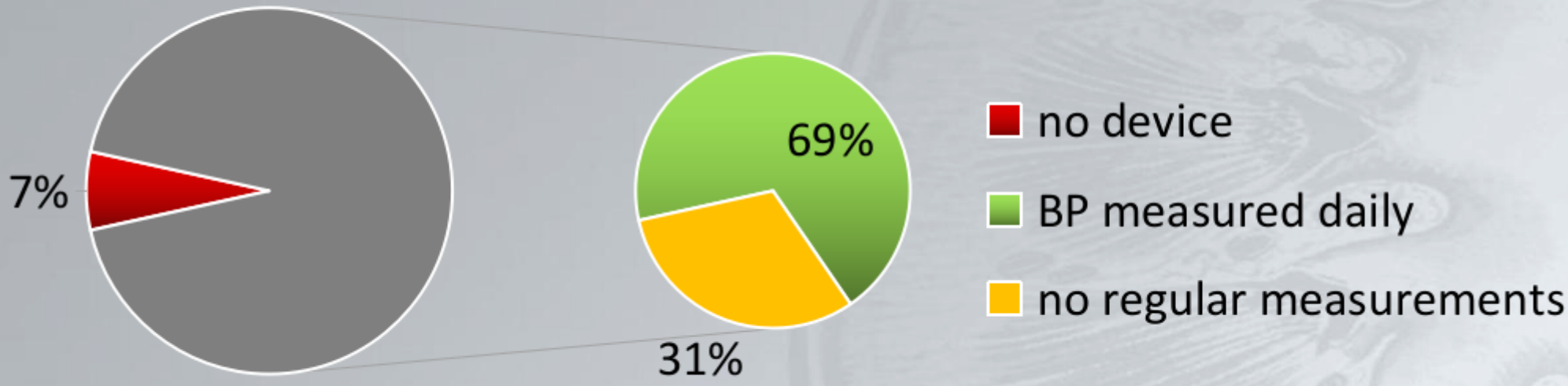
- good correlation to target-organ damage
- predictor of cardiovascular events and mortality

- best agreement with ABPM results (compared to peri-dial BP)
- helps patient education, improves adherence
- ideal for treatment follow-up

BP outside the dialysis unit: HBPM

- Many patients have BP device at home
- and measure BP on a regular basis

Why are we not using these data?



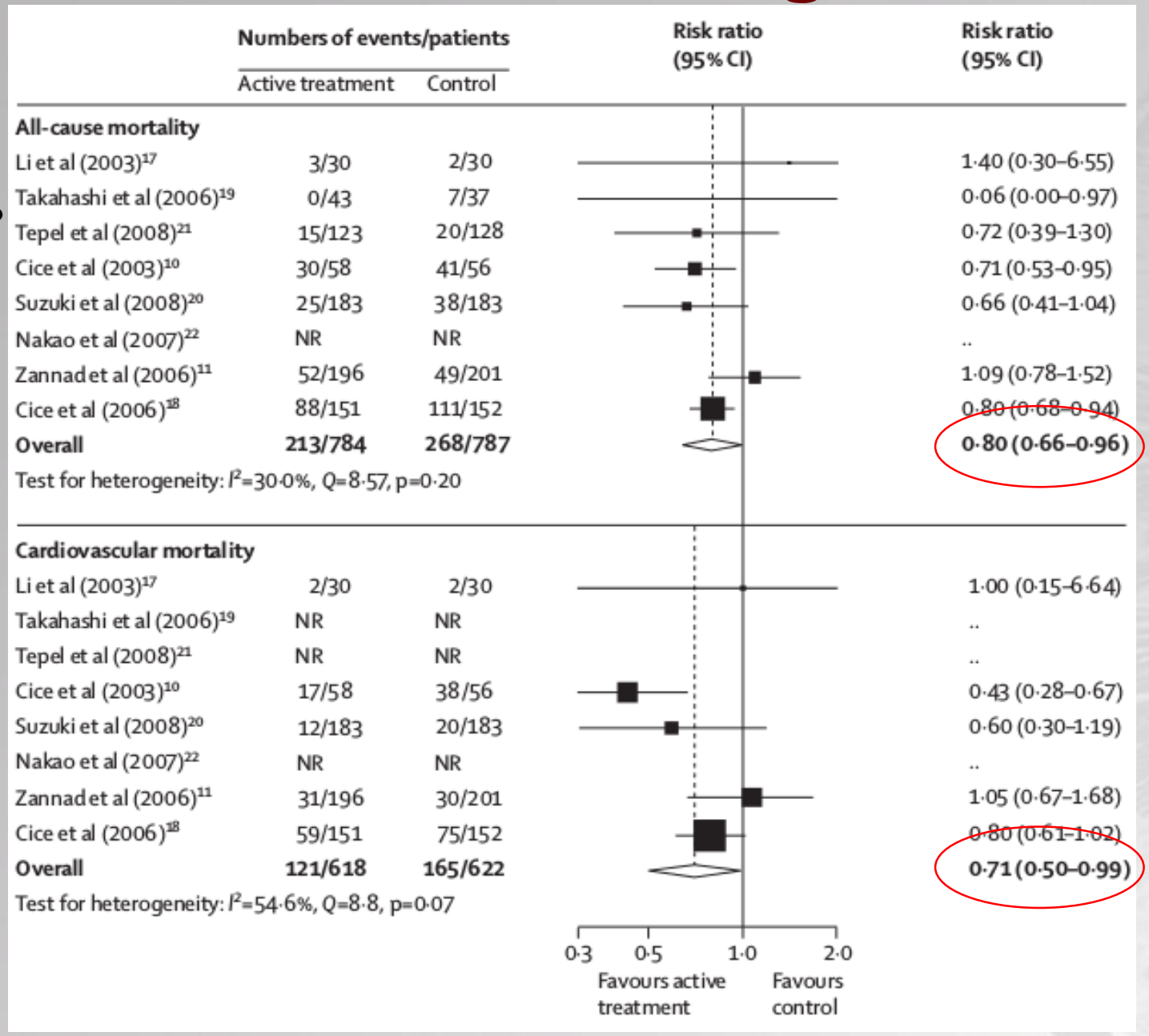
Patient's own device and technique need to be checked and validated!

single-unit survey, unpublished

Is it worth lowering BP in dialysis patients?

- Definition of HTN changing -> Treatment target changed?
- Can we still rely on old studies using peri-dialysis BP measurements?

Is it worth lowering BP in dialysis patients?



Randomized trials

(various drugs to placebo)

BP lowering associated with

20% reduction in all-cause mortality

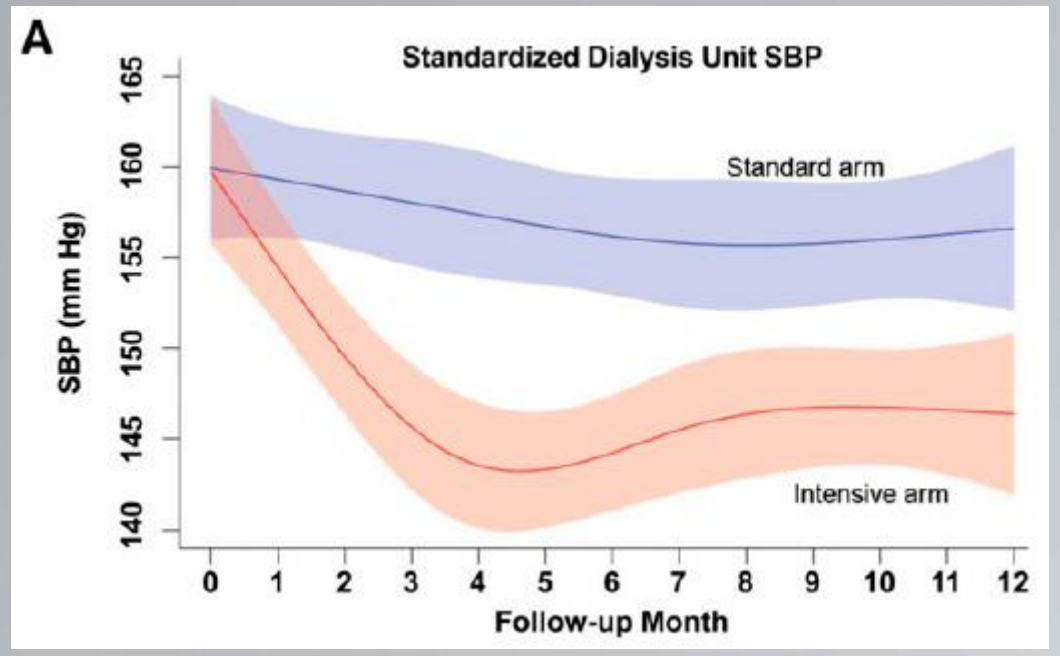
29% reduction in CV-mortality

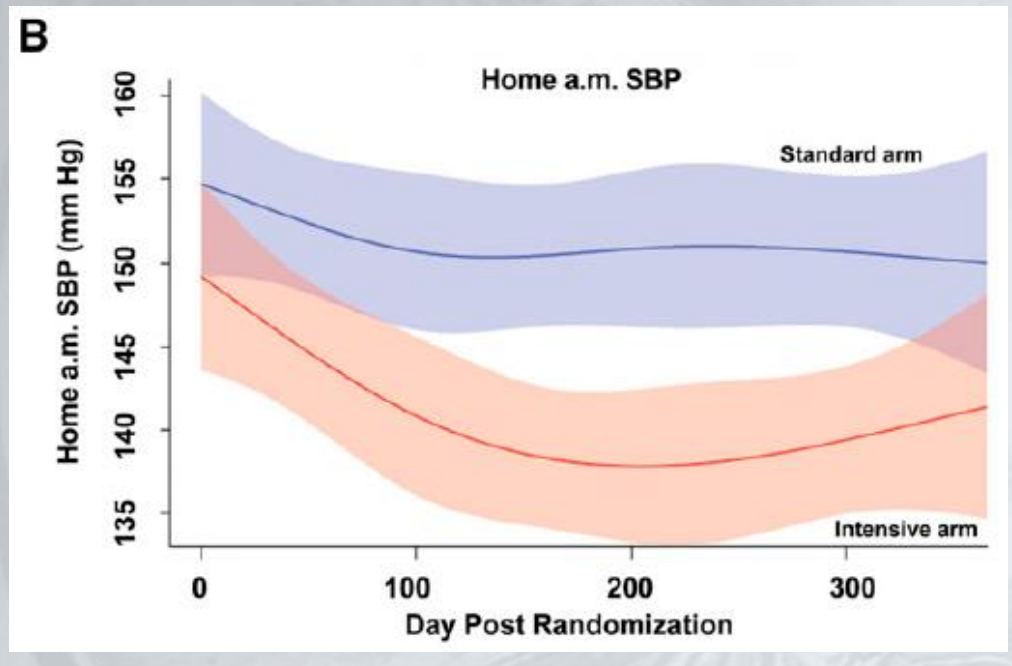
Heerspink et al, Lancet 2009; 373: 1009–15

Is it worth lowering BP in dialysis patients?

Blood pressure In Dialysis pilot study (safety & feasibility)

- prevalent chronic HD patients, predial SBP>155mmHg
- randomized: intensive (110-140mmHg) vs standard (155-165mmHg)
- 126 patients randomized





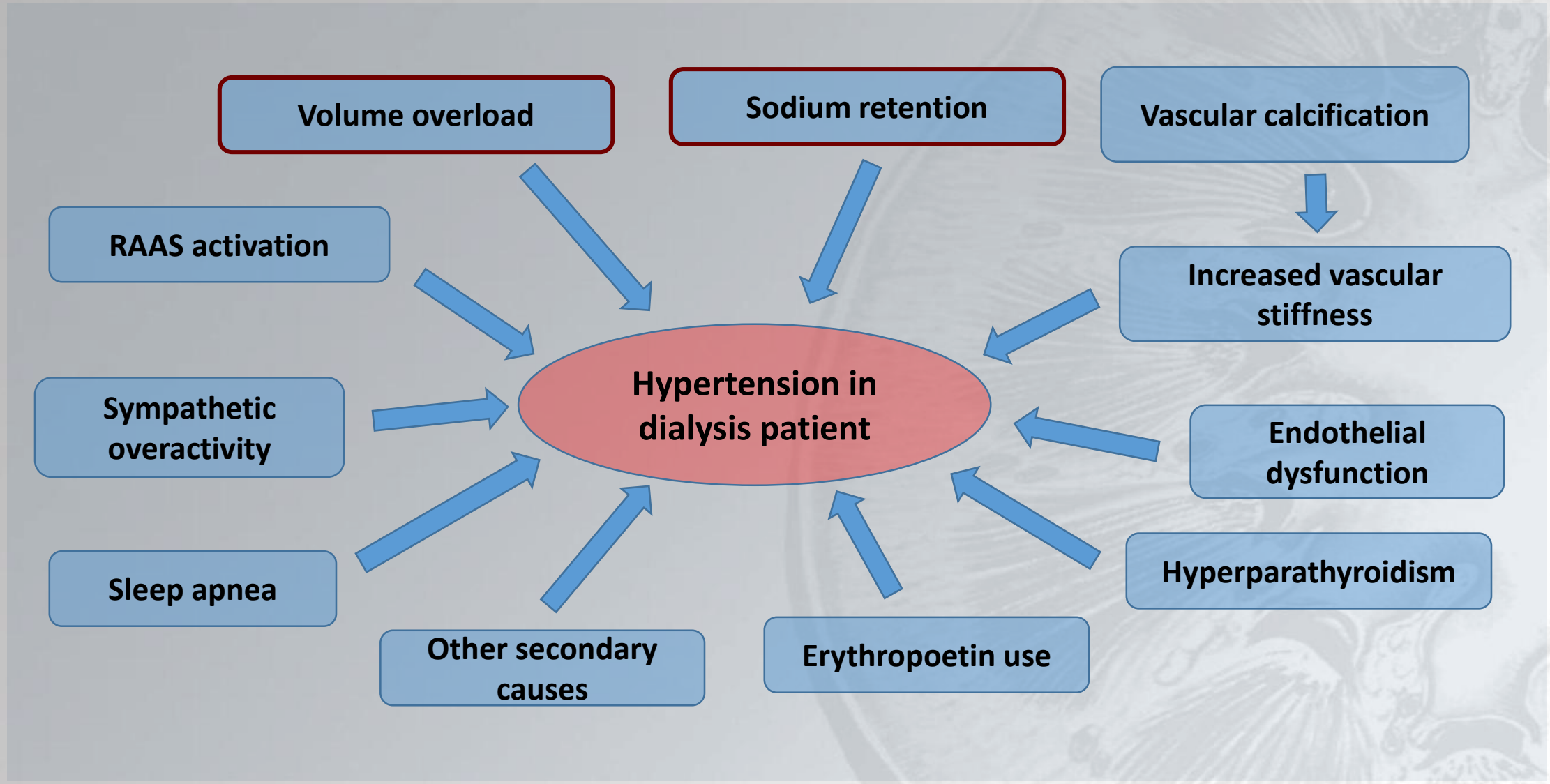
- **more patients (4 vs 1) died in the intensive arm**

Miskulin et al, J Am Soc Nephrol 29: 307–316, 2018

Is it worth lowering BP in dialysis patients?

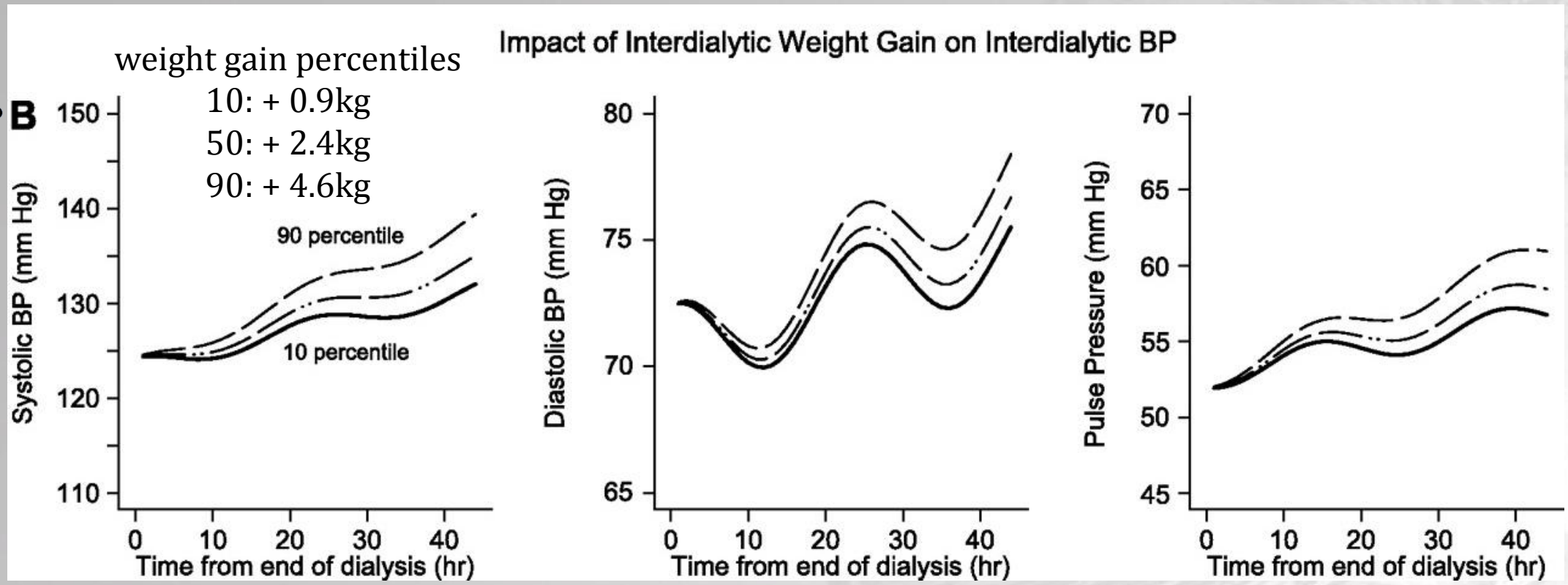
- Definition of HTN changing -> Treatment target changed?
- Can we still rely on old studies using peri-dialysis BP measurements?
- *Maybe, not yet clear, we need more ABPM / HBPM targeted studies.*

Pathophysiology of hypertension in dialysis



Interdialytic weight gain and blood pressure

Continuous water and sodium accumulation between dialysis sessions.



This changing volume status also *influences the effect of some antihypertensive agents*.

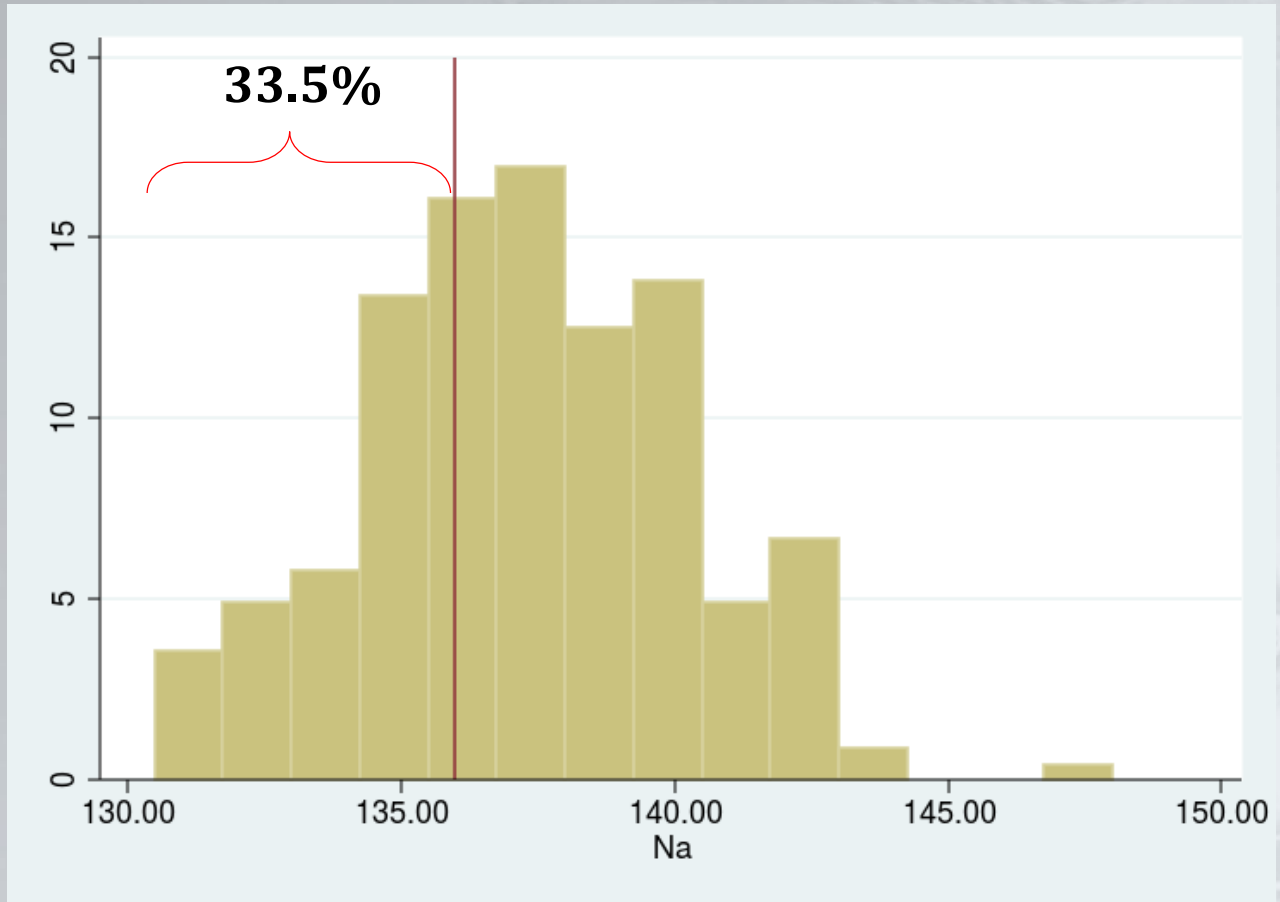
Sources of salt: dietary and dialysis !

Agarwal et al, Am J Physiol Renal Physiol 2008;294:F303-F308

Sodium retention and blood pressure

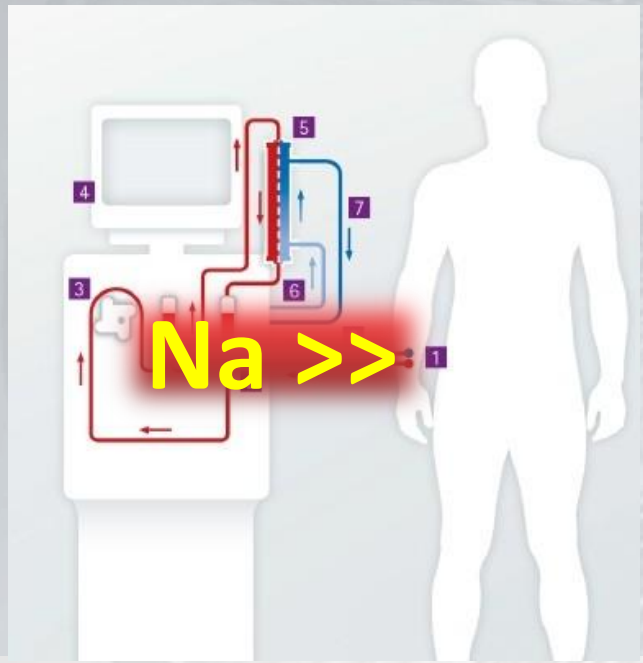
- Dialysate sodium is often not set to patient pre-dialysis Na level
  - many patients are dialyzed against a high Na bath

dialysate Na 136mmol/l



Sodium retention and blood pressure

- Dialysate sodium is often not set to patient pre-dialysis Na level
  - many patients are dialyzed against a high Na bath
- Sodium gain during dialysis → increases thirst after dialysis
  - greater interdialytic weight gain
  - increased blood pressure - *also independent of water retention*
  - more ultrafiltration on next HD
    - higher risk of hypotensive episodes



Sodium retention and blood pressure

- Dialysate sodium is often not set to patient pre-dialysis Na level
  - many patients are dialyzed against a high Na bath
- Sodium gain during dialysis → increases thirst after dialysis
  - greater interdialytic weight gain
  - increased blood pressure - *also independent of water retention*
  - more ultrafiltration on next HD
    - higher risk of hypotensive episodes

(Dialysis) people like Camel

Sodium retention and blood pressure

- Dialysate sodium is often not set to patient pre-dialysis Na level
  - many patients are dialyzed against a high Na bath
- Sodium gain during dialysis → increases thirst after dialysis
  - greater interdialytic weight gain
  - increased blood pressure - *also independent of water retention*
  - more ultrafiltration on next HD
    - higher risk of hypotensive episodes

(Dialysis) people like Camel

Dialysis machines like Salt-shaker

Sodium retention and blood pressure

- Dialysate sodium is often not set to patient pre-dialysis Na level
  - many patients are dialyzed against a high Na bath
- Sodium gain during dialysis → increases thirst after dialysis
  - greater interdialytic weight gain
  - increased blood pressure - *also independent of water retention*
  - more ultrafiltration on next HD
    - higher risk of hypotensive episodes

- Lowering dialysate sodium <u>+ low sodium diet</u>
  - improve blood pressure control
  - reduce interdialytic weight gain

?

The effect of low sodium dialysate

Reference	Intervention	BP	IDWG	Thirst	Morbidity	Mortality
Hecking 2012 (110)	Observational data (DOPPS)	Variable: facility dependent change in predialysis SBP seen	Higher with higher DNa	NA	Less hospitalizations with higher DNa	Lower in facilities using standardized DNa
Shah 2012 (106)	Lowered facility DNa followed by reaudit of clinical practice	Decreased	Decreased	NA	Less IDH seen	NA
McCausland 2011 (143)	Observational data	No association	Decreased with lower DNa	NA	NA	Increased if high DNa and SNa
Munoz-Mendoza 2011 (100)	Intra-individual period of lowered DNa compared to periods of standard DNa	Decreased	Decreased	NA	No difference IDH seen	NA
Sayarlioglu 2007 (144)	Lowered DNa with echo pre and post	Decreased	Decreased	NA	Improved echo parameters at 8 weeks	NA
Thein 2007 (95)	Facility level decrease in dialysate sodium	Decreased	No change	NA	No difference IDH seen	NA
Lambie 2005 (92)	Effective lowering DNa Randomized trial	Decreased	Decreased	Trend to decrease	Increased IDH in treatment group	NA
De-Paula 2004 (102)	Individualized DNa Single blind crossover	Decreased (if HPT at baseline)	Decreased	Decreased	NA	NA

DNa, dialysate sodium; SNa, serum sodium; HPT, hypertensive; IDH, intradialytic hypotension; NA, not assessed.

Lewicki et al, Semin Dial. 2013;26(1):62-72.

The effect of low sodium dialysate

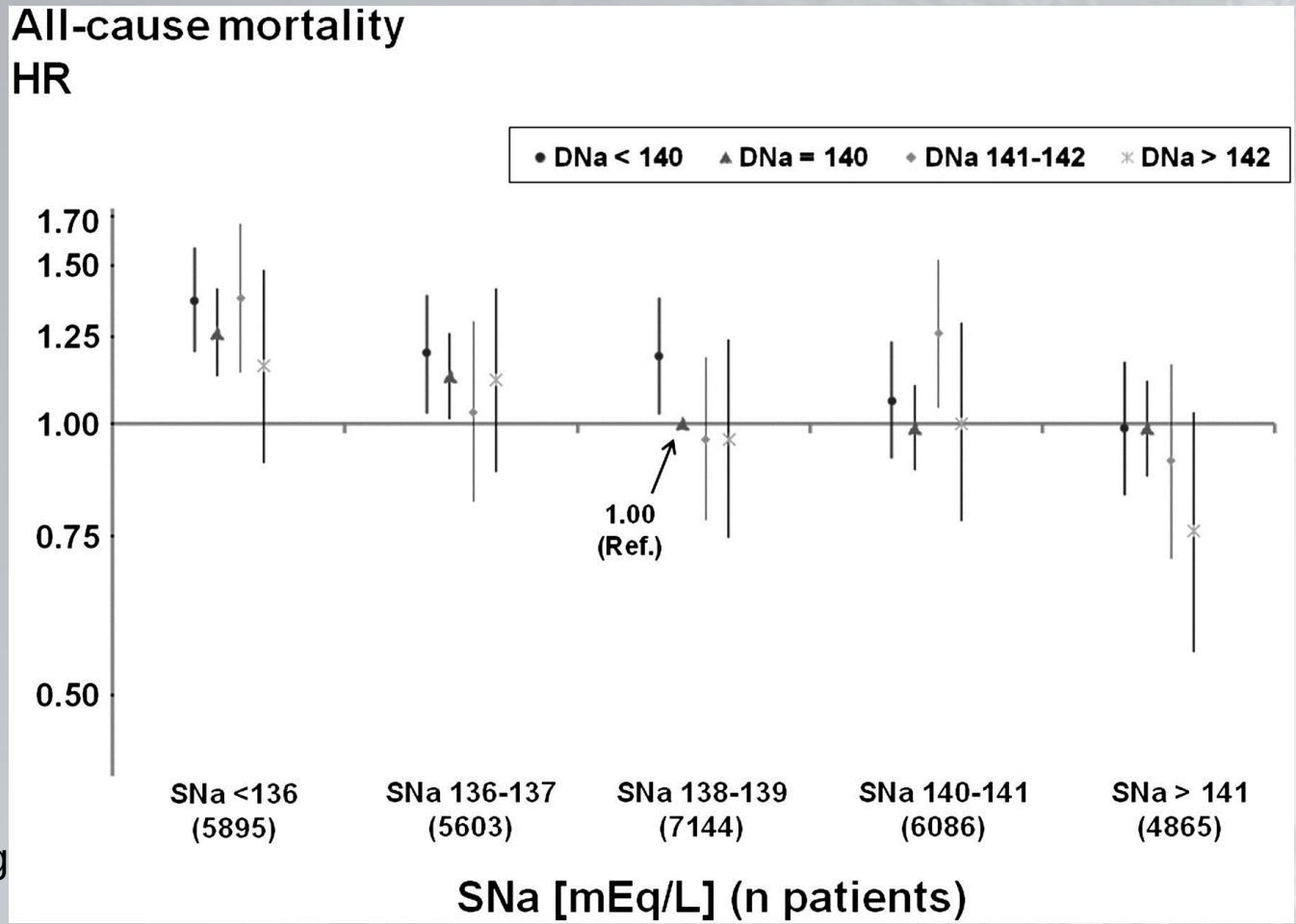
DOPPS analysis

n=29593

higher mortality with

low se Na + low dial Na !!

adjusted for age, sex, body mass index, diabetes and 13 other comorbid conditions, residual renal function, vascular access, serum albumin, hemoglobin, ferritin, serum creatinine, white blood cell count, and facility clustering



Hecking et al. CJASN 2012;7:92-100

The effect of low sodium dialysate

Systematic review of 23 studies (n=76635)

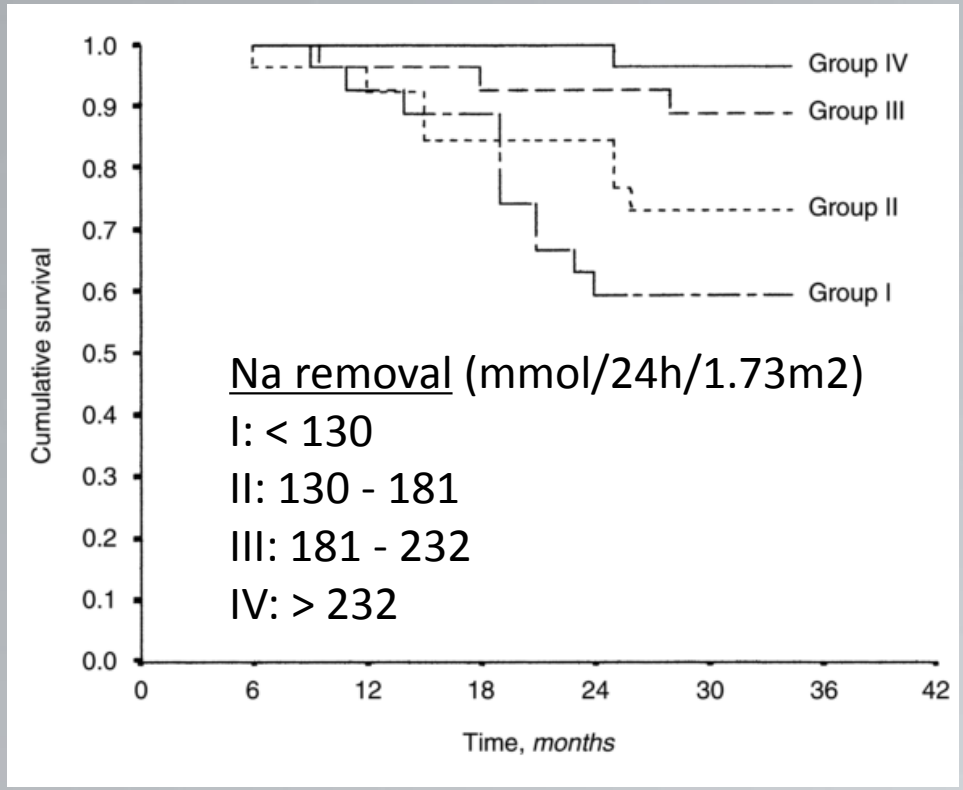
- heterogenous studies
- inconclusive results
- low quality evidence

Basile et al, Nephrol Dial Transplant (2016) 31: 548–563

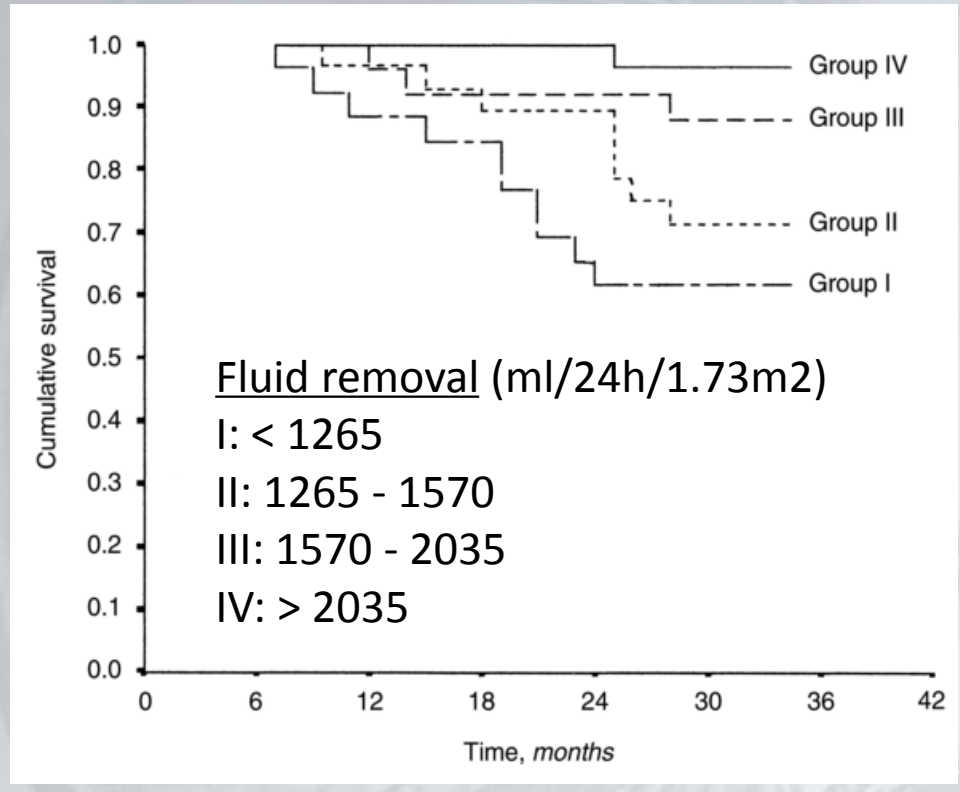
The effect of low sodium dialysate

Observational study, 125 patients on PD, follow-up: 3 years

Total Sodium removal



Total fluid removal



Ateş et al, Kidney International. 2001;60:767-776.

Low sodium dialysate ?

Risk of lowering

- muscle cramps
- intradialytic hypotension -> inferior outcome ?

- careful and slow adjustment of dialysate Na close to serum Na ?
  in hypertensive dialysis patients

- *More evidence is needed.*

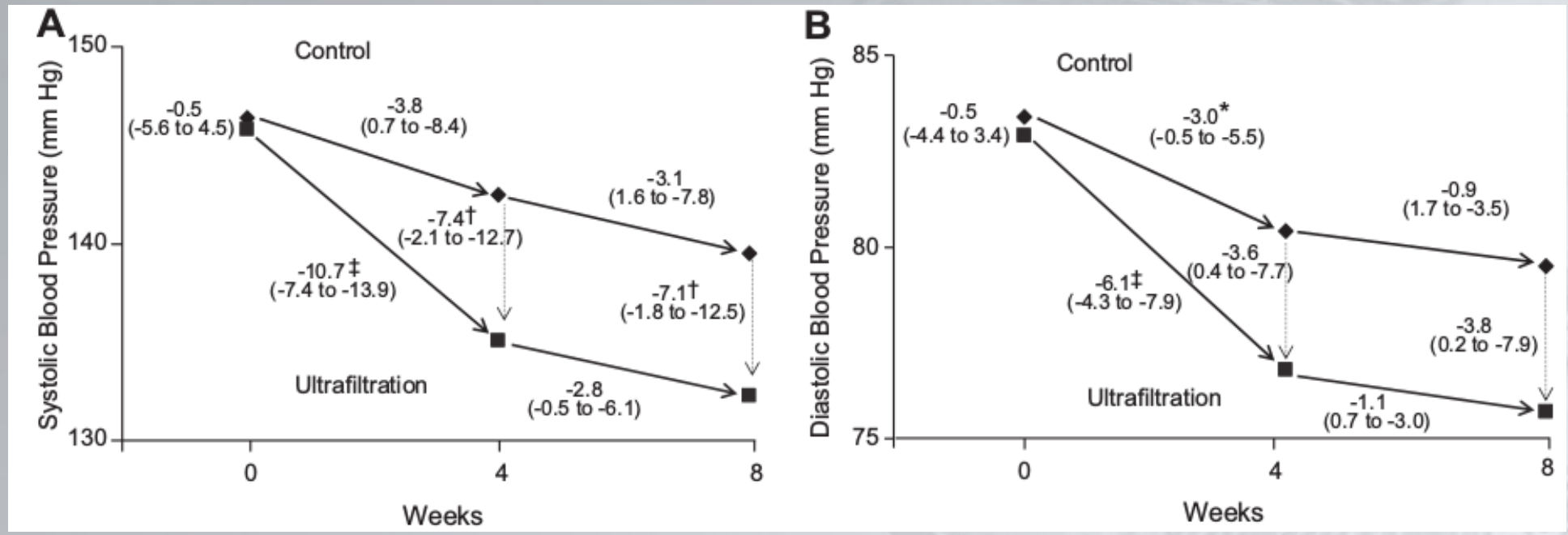
Ateş et al, Kidney International. 2001;60:767-776.

Control of volume overload and hypertension

The importance of dry-weight reduction to control hypertension

DRIP Trial: HD patients with hypertension

- RCT: additional ultrafiltration (n=100) vs control (n=50)
- 44h ABPM for blood pressure evaluation

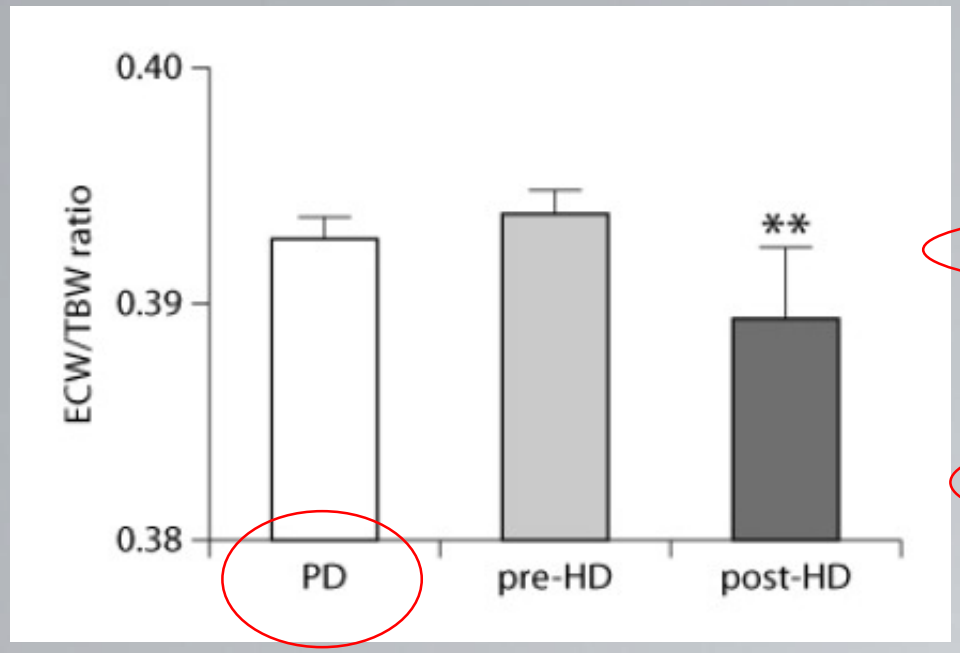


Agarwal et al, Hypertension. 2009;53(3):500-507.

Volume overload on peritoneal dialysis

Volume overload is very common in PD patients linked to

- loss of residual kidney function
- number of antihypertensive medications



Variable	r value	P value
TBW (L)	-0.17	<0.0001
ECW (L)	0.153	0.0002
Number of different BP meds prescribed	0.249	0.0003
Prescription of ≥22.7 g/L glucose dialysate	0.13	0.0014
Age (years)	0.119	0.0036
Intracellular water (L)	-0.098	0.0158
Daily urine volume (L)	-0.1022	0.0149
Fat weight (kg)	0.085	0.037
Log CRP (mg/L)	0.04	0.04

*

Fan et al, Int J Artif Organs. 2012;35(5):338-345.
Papakrivopoulou et al, Nephron Extra. 2012 Jan-Dec; 2(1): 48–54.

Volume overload on peritoneal dialysis

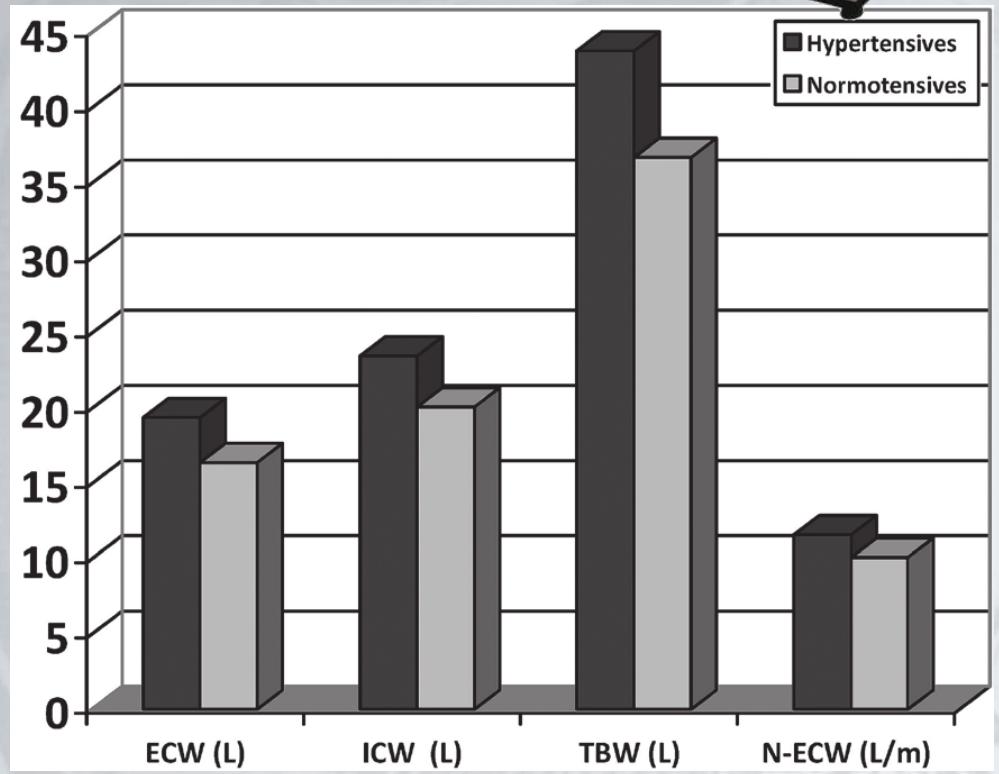
Volume overload is very common in PD patients linked to

- **hypertension**

TABLE III Body weight and fluid status in the patient groups

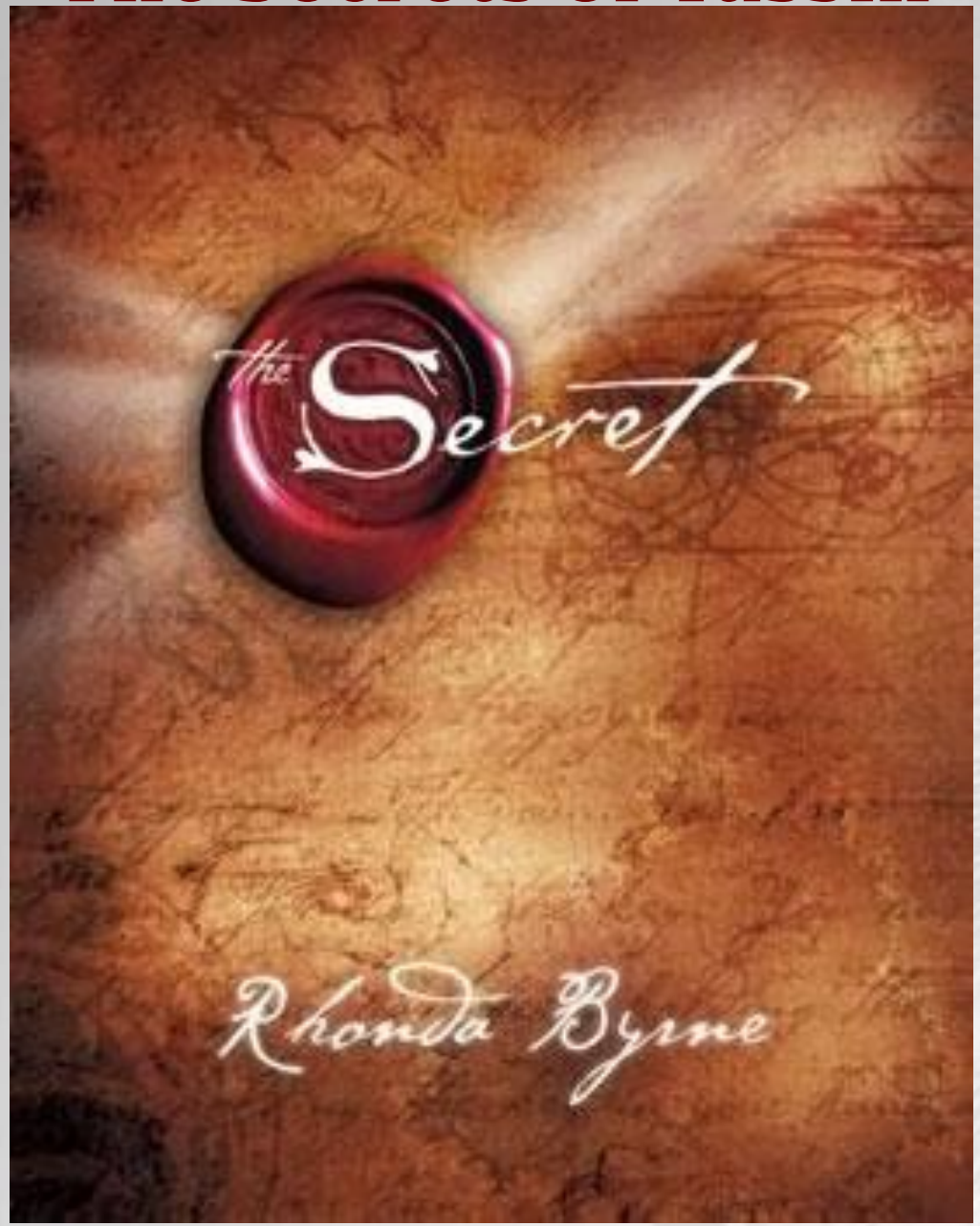
Variable	Hypertensive? Yes	Hypertensive? No	p Value
Weight (kg)	77.3±20.3	64.5±9.8	**0.05**
ECW (L)	19.4±4.3	16.4±3.5	**0.03**
ICW (L)	23.5±6.6	20.1±5.5	0.12
TBW (L)	43.8±11.5	36.7±9.4	**0.05**
nECW (L/m)	11.6±1.9	10.1±1.8	**0.03**

ECW = extracellular water; ICW = intracellular water; TBW = total body water; nECW = extracellular water normalized to height in meters.



Inal et. al, Advances in Peritoneal Dialysis, Vol. 28, 2012

The Secrets of Tassin



The Secrets of Tassin

The effect of long dialysis, sodium restriction and ultrafiltration

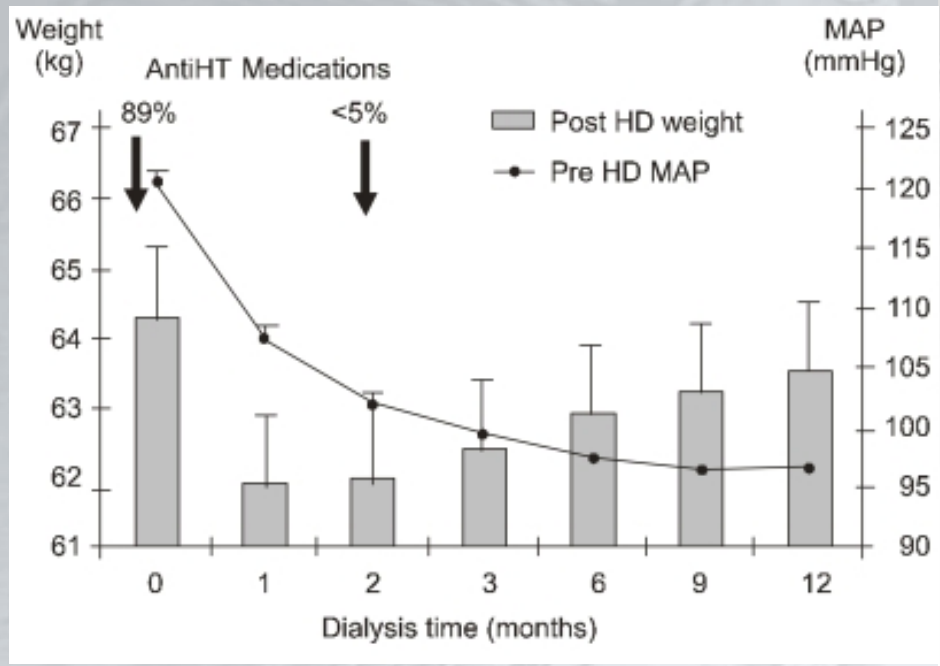
- 692 HD patients in Tassin, France
- long dialysis sessions: 3x8h
- dialysate sodium: 138mmol/l
- sodium restriction: 4-5g/day !
  - low sodium bread from dialysis unit
- aggressive dry-weight reduction within 2-3 months

Charra et al, Blood Purif 1994; 12:252.
Charra et al, Hemodial Int. 2007 Jan; 11(1):21-31.

The Secrets of Tassin

The effect of long dialysis, sodium restriction and ultrafiltration

- 692 HD patients in Tassin, France
- long dialysis sessions: 3x8h
- dialysate sodium: 138mmol/l
- sodium restriction: 4-5g/day !
  - low sodium bread from dialysis unit
- aggressive dry-weight reduction within 2-3 months
- <u>98.4% of patients do not require antihypertensive medication</u>



Charra et al, Blood Purif 1994; 12:252.
Charra et al, Hemodial Int. 2007 Jan; 11(1):21-31.

Aggressive ultrafiltration for all patients?

- Aggressive ultrafiltration → <u>early loss of residual kidney function</u>
- *Residual renal function is of paramount importance !*
  - survival advantage
  - better blood pressure control
  - better control of renal anemia and bone-mineral disorder
  - lower inflammation
  - greater quality of life

Aggressive ultrafiltration for all patients?

- Aggressive ultrafiltration → <u>early loss of residual kidney function</u>
- *Residual renal function is of paramount importance !*
  - survival advantage
  - better blood pressure control

Oh, my patient has volume overload !

Easy, ultrafiltration will take care of it !

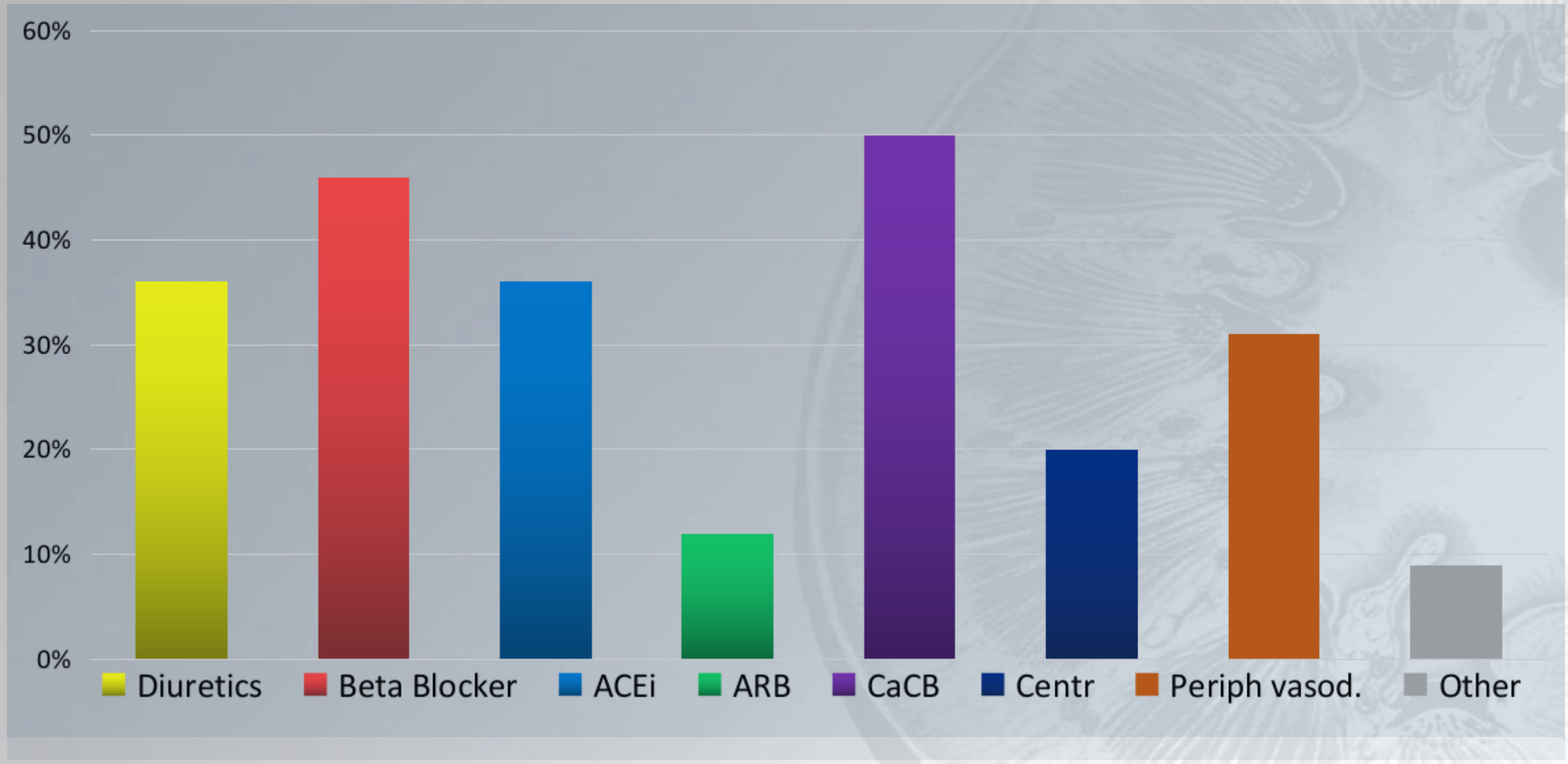
Aggressive ultrafiltration for all patients?

- Aggressive ultrafiltration → <u>early loss of residual kidney function</u>
- *Residual renal function is of paramount importance !*
  - survival advantage
  - better blood pressure control
  - better control of renal anemia and bone-mineral disorder
  - lower inflammation
  - greater quality of life

- Methods for controlling hypervolemia, lowering dry-weight
  - aggressive ultrafiltration - for anuric patients
  - <u>non-anuric patients: use more diuretics !</u>

Antihypertensive therapy in real-world

multicenter cross-sectional survey, n=323



Ambrus, unpublished

Diuretics in dialysis patients

Ineffective for blood pressure control, per se.

- useful for
  - reaching euvolemic state / dry weight
  - preservation of residual kidney function
    - better control of CKD-MBD
    - better outcome
- loop diuretics: furosemid
  - administer high enough single dose (160-250 ? 500mg)
- thiazides
  - ineffective alone
  - can enchance the effect of furosemid even in patients on dialysis

Diuretics in dialysis patients

	Usual dose	Excretion	GFR < 10 ml/min	Removal with dialysis		Supplement for dialysis
				Hemodialysis	Peritoneal dialysis	
Diuretics						
Acetazolamide	250 mg q6–8 h	K	Avoid	Unknown	Unknown	Not applicable
Amiloride	5–10 mg q.d.	K	Avoid	N/A	N/A	Not applicable
Bumentanide	0.5–2 mg q8–12 h	K	100%	None	None	None
Chlorthalidone	30–60 mg q.d.	K	Avoid	N/A	N/A	Not applicable
Ethacrynic acid	50–100 mg b.i.d.	L (K)	Avoid	None	None	Not applicable
Furosemide	40–80 mg b.i.d.	K (L)	100%	None	None	None
Hydrochlorothiazide	25–50 mg q.d.	K	Avoid	None	None	Not applicable
Indapamide	2.5 mg q.d.	K	Avoid	None	None	Not applicable
Metolazone	5–10 mg q.d.	K (L)	100%	None	None	None
Spironolactone	50–100 mg q.d./b.i.d.	K (L)	Avoid	N/A	N/A	Not applicable
Torsemide	5–10 mg b.i.d.	L (K)	100%	Avoid	Avoid	None
Trimaterene	25–50 mg b.i.d.	K	Avoid	N/A	N/A	Not applicable

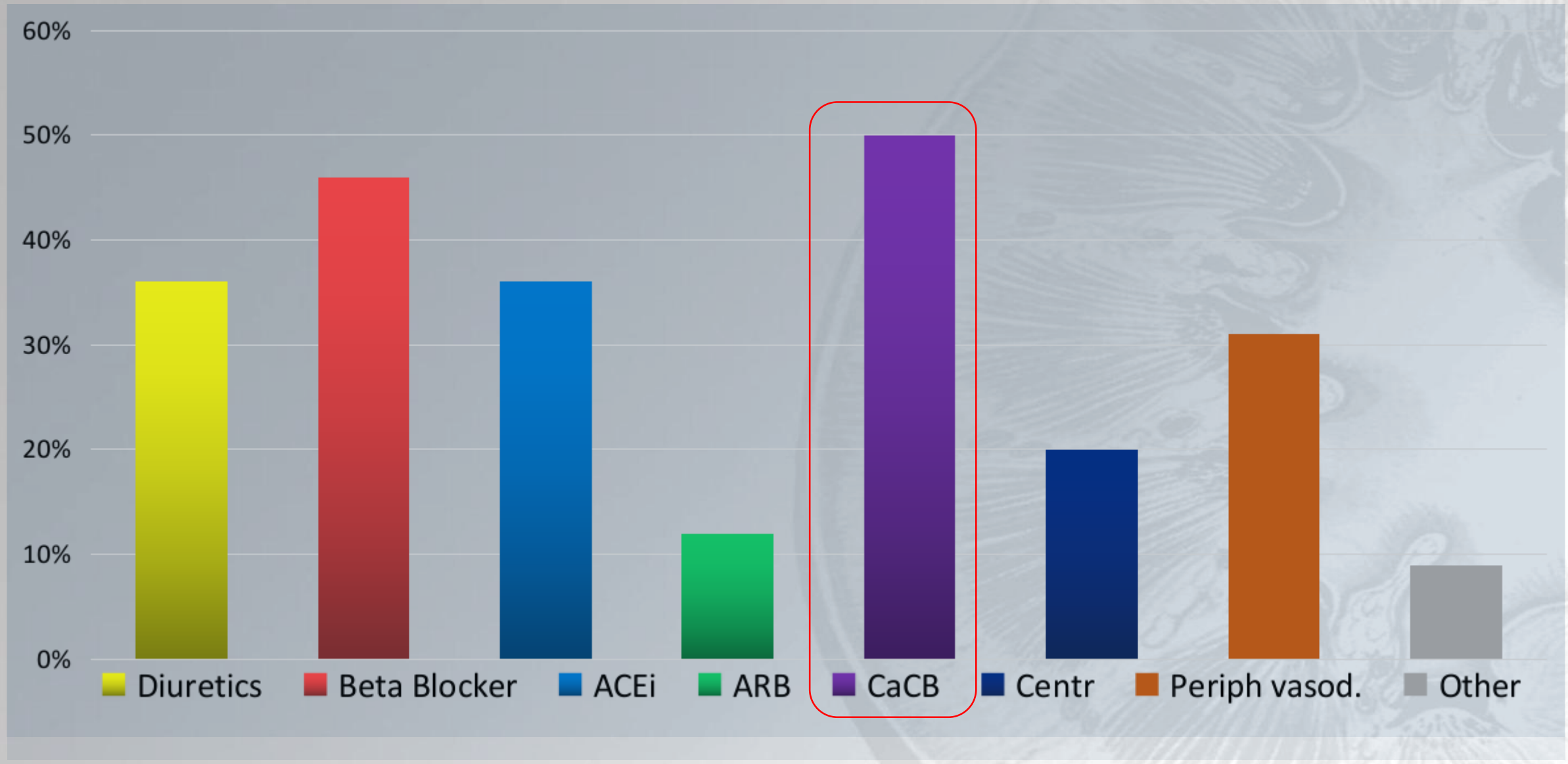
?

Should we really avoid using: thiazide / spironolactone ?

Levin et al, Kidney Int. 2010;77(4):273-284.

Antihypertensive therapy in real-world

multicenter cross-sectional survey, n=323



Ambrus, unpublished

Calcium channel blockers

Ideal antihypertensive drugs in dialysis patients.

Unchanged pharmacokinetics in ESRD.

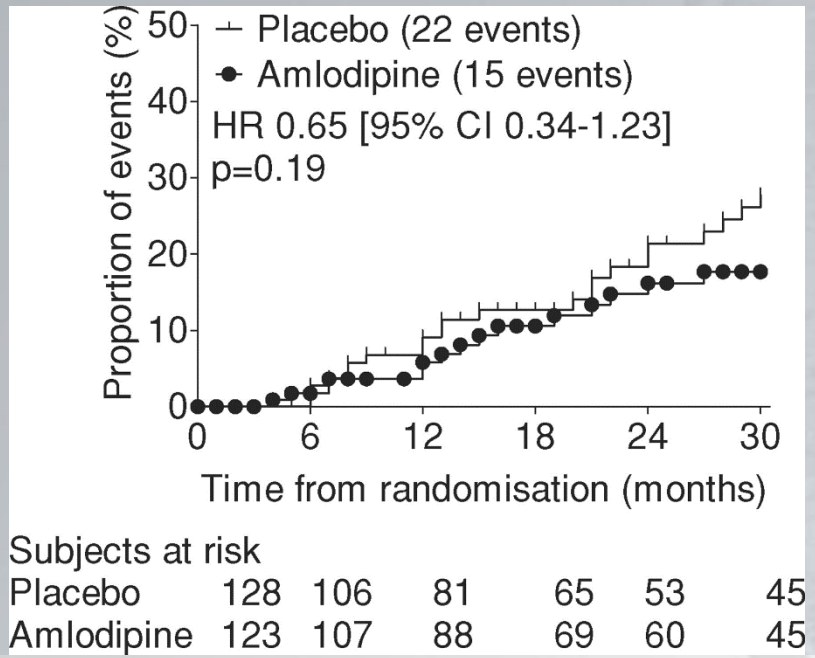
Effective in patients with volume overload.

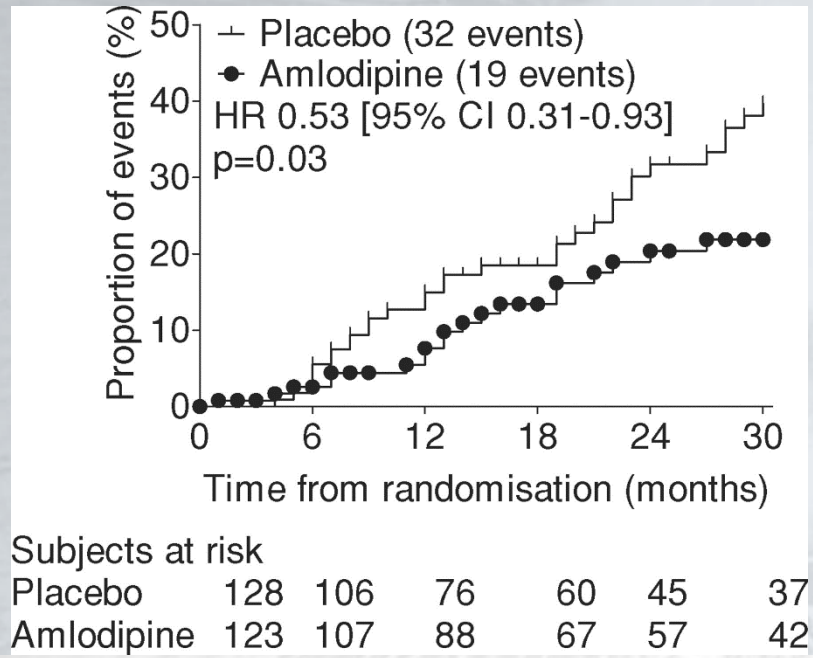
	Usual dose	Excretion	GFR < 10 ml/min	Removal with dialysis		Supplement for dialysis
				Hemodialysis	Peritoneal dialysis	
CCB						
Amlodipine	2.5–10 mg q.d.	L	100%	None	None	None
Diltiazem CD	180–360 mg	L (K)	100%	None	None	None
Felodipine	5–10 mg q.d.	L	100%	None	None	None
Isradipine	2.5–10 mg b.i.d.	L	100%	None	None	None
Lacidipine	2–6 mg/day	L (K)	100%	None	None	None
Manidipine	10–20 mg/day	L	100%	None	None	None
Nicardipine	20–40 mg t.i.d.	L	100%	None	None	None
Nifedipine XL	30–90 mg q.d.	L	100%	None	None	None
Nimodipine	30 mg q8 h	K (L)	100%	None	None	None
Nisoldipine	10 mg b.i.d.	K (L)	100%	None	None	None
Nitrendipine	20 mg b.i.d.	L (K)	100%	None	None	None
Verapamil CD	180–360 mg q.d.	L	100%	None	None	None

Calcium channel blockers

Do they also lower mortality?

- randomized trial, 251 HD patients with hypertension
  - amlodipine 10mg daily vs placebo
  - follow-up: 30 months
  - no effect on mortality, but reduced CV events (due to antihypertensive effect?)





Tepel et al, Nephrol Dial Transplant. 2008;23(11):3605-3612.

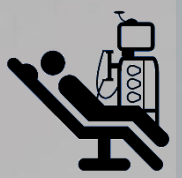
Beta-blockers in dialysis patients

	Usual dose	Excretion	GFR < 10 ml/min	Removal with dialysis		Supplement for dialysis
				Hemodialysis	Peritoneal dialysis	
β-blockers						
Acebutolol	400–600 mg q.d./b.i.d.	L (K)	30–50%	30%	None	150 mg
Atenolol	50–100 mg q.d.	K (L)	25–50%	50%	None	25–50 mg
Betaxolol	10–20 mg q.d.	L	50%	None	None	None
Bisoprolol	2.5–20 mg q.d.	L	100%	None	None	None
Carvedilol	25 mg b.i.d.	L (K)	50%	None	Unknown	None
Esmolol	50–150 µg/kg/min i.v.	L	100%	None	None	None
Labetalol	200–600 mg b.i.d.	K (L)	100%	None	None	None
Metoprolol	50–100 mg b.i.d.	K (L)	100%	None	None	50 mg
Nadolol	80–100 mg b.i.d.	K	25%	50%	None	80 mg
Pindolol	10–40 mg b.i.d.	K (L)	100%	None	None	None
Propanolol	80–160 mg b.i.d.	K	100%	None	None	None
Sotalol	160 mg q.d.	K	15–30%	50%	None	50 mg
Timolol	10–20 mg b.i.d.	L (K)	100%	None	None	None

First or second line therapy in dialysis patients
partly due to cardiovascular co-morbidity

Levin et al, Kidney Int. 2010;77(4):273-284.

Beta-blockers in dialysis patients



Reduction in mortality, CV morbidity and risk of sudden death

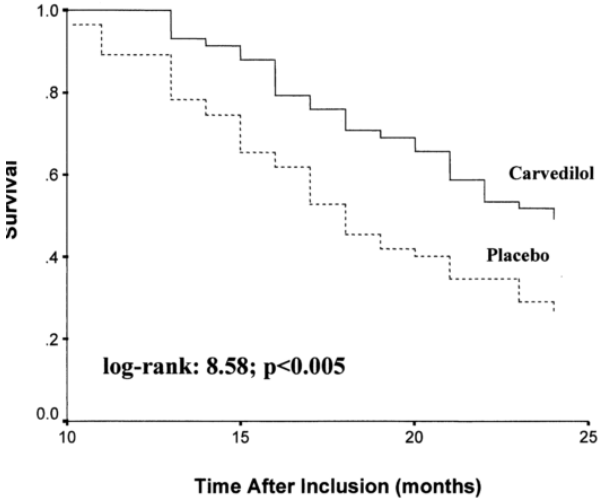
- DOPPS, observational, 37765 patients, 12 countries

  lower risk of sudden death in patients using beta-blockers:
  HR 0.88 (95% CI: 0.78-0.99, p=0.03)

- randomized trial, 114 HD patients with DCM
  - carvedilol vs placebo

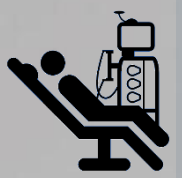
Table 3. Secondary End Points and Exploratory Analyses

	Placebo (n = 56)	Carvedilol (n = 58)	Hazard Ratio (95% CI)	p Value
Secondary End Points				
All-cause mortality	41 (73.2%)	30 (51.7%)	0.51 (0.32–0.82)	< 0.01
All-cause hospital admission	33 (58.9%)	20 (34.5%)	0.44 (0.25–0.77)	< 0.005
All cardiovascular deaths	38 (67.9%)	17 (29.3%)	0.32 (0.18–0.57)	< 0.0001
Non-fatal myocardial infarction	1 (1.8%)	0 (0%)	0.81 (0.61–1.34)	0.31
Combined end point	39 (69.6%)	17 (29.3%)	0.76 (0.47–1.22)	0.22
Permanent treatment withdrawals	15 (26.8%)	17 (29.3%)	1.12 (0.84–1.24)	0.68



Jadoul et al, Clin J Am Soc Nephrol. 2012;7(5):765-774.
Cice et al, J Am Coll Cardiol. 2003;41(9):1438-1444.

Beta-blockers in dialysis patients



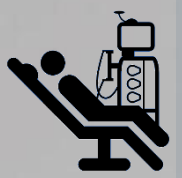
Are they also good antihypertensives?

- randomized trial (pilot), 25 HD patients with intradial hypertension
  - carvedilol titrated to 50mg bid vs placebo, follow-up: 12 weeks
  - decreased SBP on ABPM by 7.5mmHg
  - improved endothel dependent flow-mediated vasodilation
  - *reduced occurence of intradialytic hypertension*

	Baseline (n=25)	Study End (n=25)	Mean Change from Baseline to Study end	P Value
Ambulatory BP (mmHg)				
systolic (44-hr)	155.4 (±14.2)	147.7 (±16.2)	−7.5 (±16.8)	0.04
daytime systolic	155.7 (±14.9)	146.9 (±15.9)	−8.2 (±18.5)	0.04
nighttime systolic	155.6 (±16.4)	149.8 (±19.7)	−4.1 (±18.2)	0.3
diastolic (44-hr)	82.4 (±10.8)	77.7 (±9.7)	−4.2 (±7.7)	0.01
daytime diastolic	83.2 (±11.8)	77.6 (±9.7)	−4.7 (±8.8)	0.02
nighttime diastolic	80.9 (±10.6)	77.0 (±11.1)	−2.8 (±7.3)	0.09

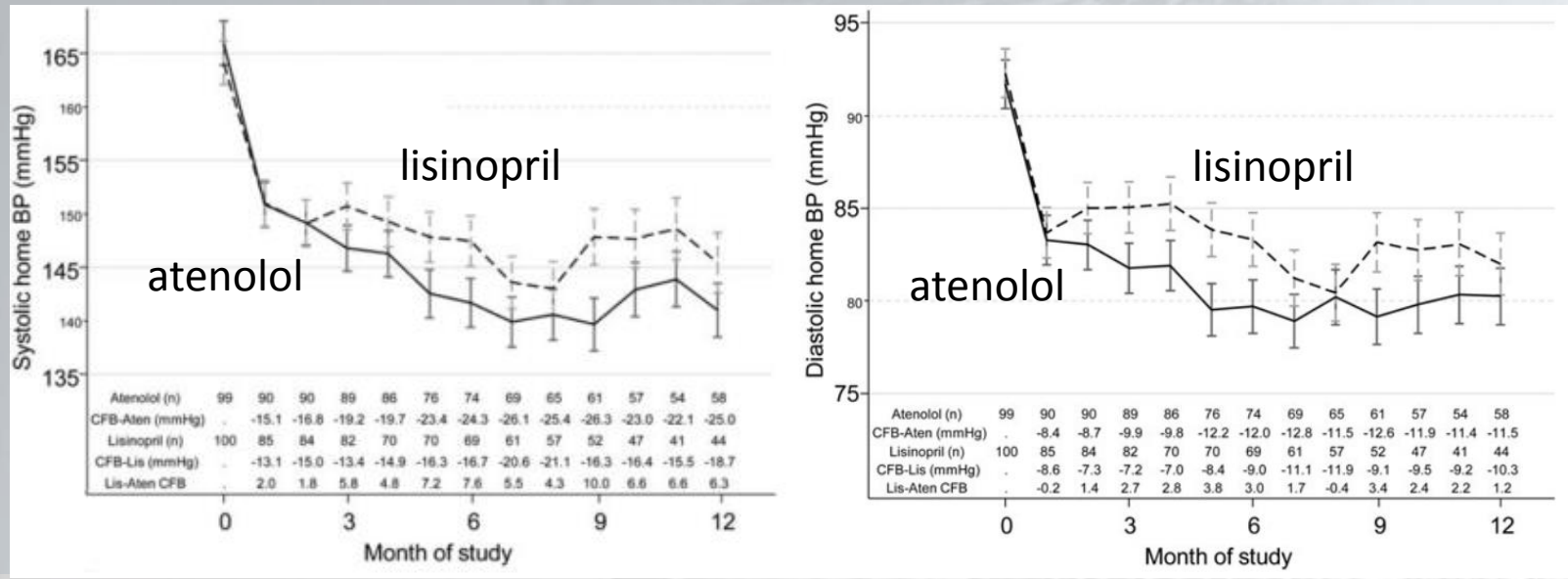
Inrig et al, Clin J Am Soc Nephrol. 2012;7(8):1300-1309.

Beta-blockers in dialysis patients



Are they also good antihypertensives?

- HDPAL, randomized trial, 200 HD patients with HTN and LVH
  - atenolol 25-100mg vs lisinopril 10-40mg three times weekly
  - no difference in SBP and DBP on ABPM or home BP control lisinopril group needed dry-weight reduction and "rescue" therapy
  - higher incidence of CV events with lisinopril



Agarwal et al, Nephrol Dial Transplant. 2014;29(3):672-681.

Beta-blockers in dialysis patients

	Usual dose	Excretion	GFR < 10 ml/min	Removal with dialysis		Supplement for dialysis
				Hemodialysis	Peritoneal dialysis	
β-blockers						
Acebutolol	400–600 mg q.d./b.i.d.	L (K)	30–50%	30%	None	150 mg
Atenolol	50–100 mg q.d.	K (L)	25–50%	50%	None	25–50 mg
Betaxolol	10–20 mg q.d.	L	50%	None	None	None
Bisoprolol	2.5–20 mg q.d.	L	100%	None	None	None
Carvedilol	25 mg b.i.d.	L (K)	50%	None	Unknown	None
Esmolol	50–150 µg/kg/min i.v.	L	100%	None	None	None
Labetalol	200–600 mg b.i.d.	K (L)	100%	None	None	None
Metoprolol	50–100 mg b.i.d.	K (L)	100%	None	None	50 mg
Nadolol	80–100 mg b.i.d.	K	25%	50%	None	80 mg
Pindolol	10–40 mg b.i.d.	K (L)	100%	None	None	None
Propanolol	80–160 mg b.i.d.	K	100%	None	None	None
Sotalol	160 mg q.d.	K	15–30%	50%	None	50 mg
Timolol	10–20 mg b.i.d.	L (K)	100%	None	None	None

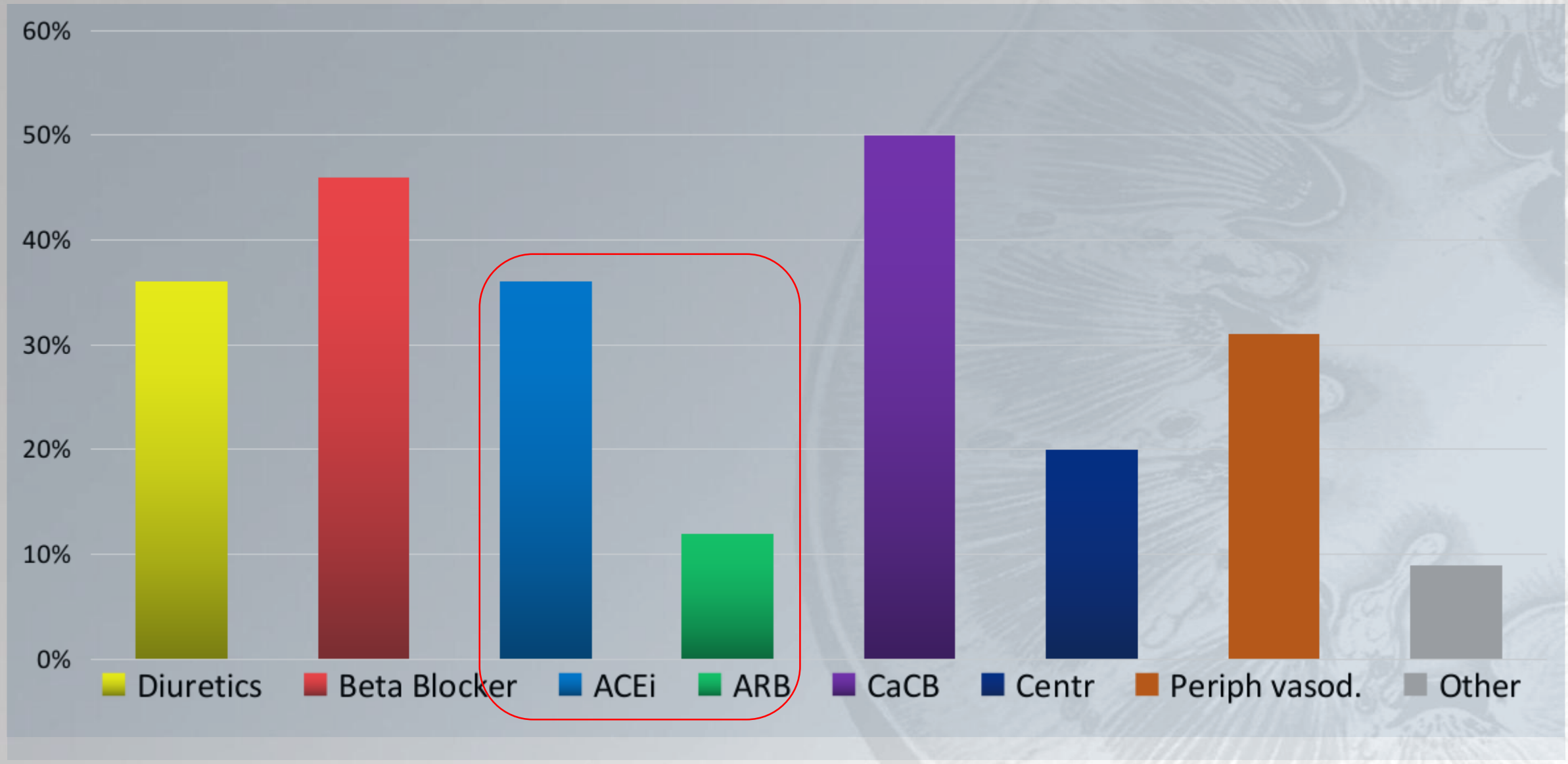
Differences in removal with hemodialysis: atenolol, sotalol can be dialyzed.

The use non-dialysable beta-blockers is advised.

Levin et al, Kidney Int. 2010;77(4):273-284.

Antihypertensive therapy in real-world

multicenter cross-sectional survey, n=323



Ambrus, unpublished

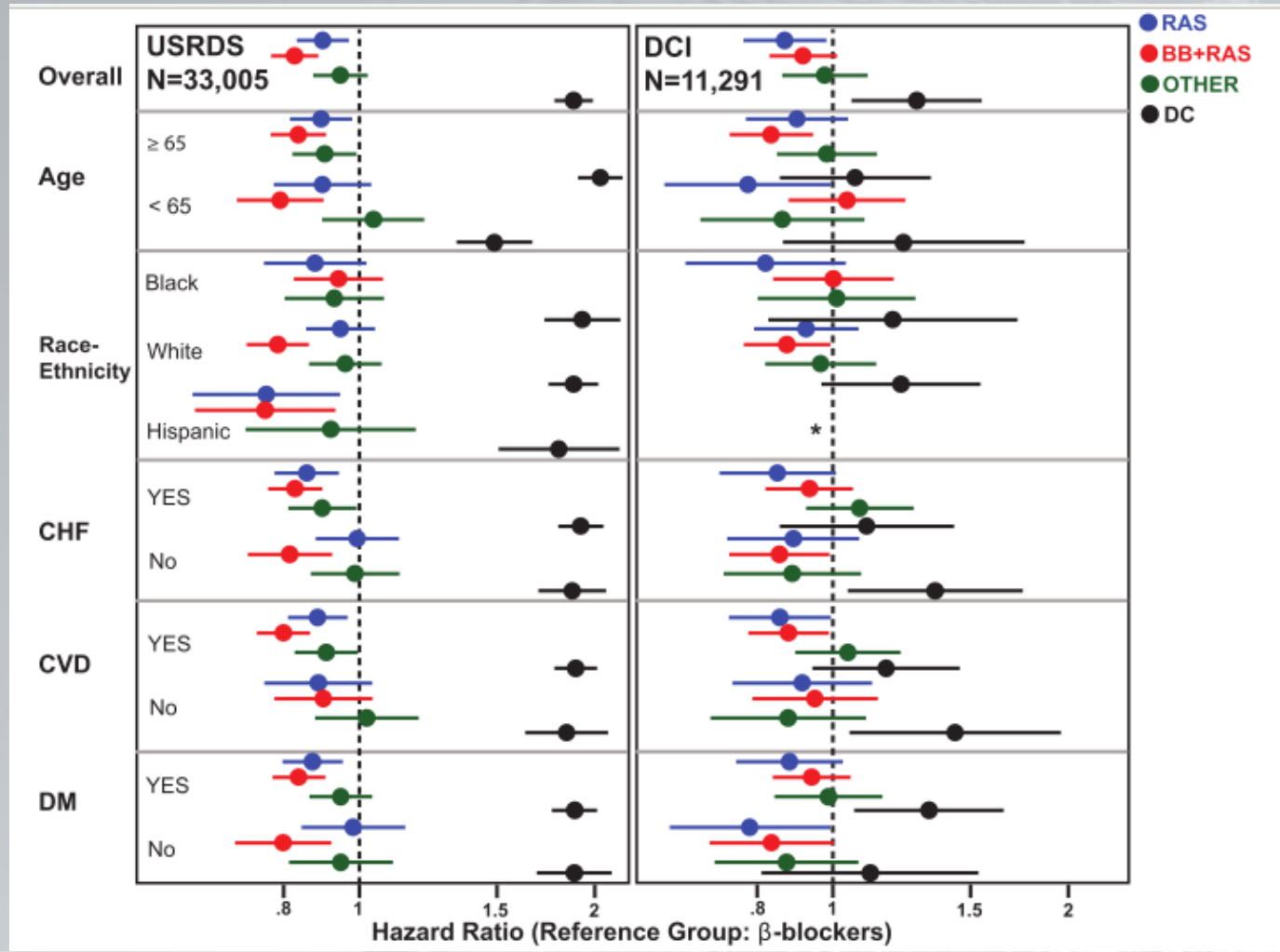
ACE inhibitors and ARBs

- first-line therapy in non CKD, also in patients with CKD
- in patients on dialysis: not convincing benefit, conflicting results

author	year	n	ACEI/ARB	design	f/u	outcome
Zannad	2006	397	fosinopril	pts with LVH, HTN was not criteria	24	CV events: no difference
Takahashi	2006	80	candesartan	not hypervolemic patients! HTN was not criteria	36	lower CV event rate
Suzuki	2008	360	losartan, valsartan, candesartan	pts **with hypertension**	36	lower CV death & event rate
Iseki	2013	469	olmesartan	pts **with hypertension**	42	CV events: no difference
Cice	2010	332	telmisartan	pts with CHF, LVEF <40% **telmisartan ADDED to ACEI**	36	lower CV death & CV event rate

ACE inhibitors and ARBs vs beta-blocker ACEi/ARB

- USRDS & Dialysis Clinic Inc. (DCI) cohort study
- n=33005 & 11291
- beta-blocker monotherapy vs
  - ACEI/ARB
  - beta-blocker+ACEI/ARB
  - other medication
- **better survival with addition of ACE / ARB**



Shafi et al, Medicine (Baltimore). 2017;96(5):e5924.

ACE inhibitors and ARBs in patients on PD ACEi/ARB

- USRDS cohort study, n=4879
- ACEI/ARB use (42%) vs non-use
- all-cause mortality: 17% relative risk reduction
- CV death: 26% relative risk reduction

Outcome	Analysis	Exposure group	Follow-up time (years)		Incidence rate (per 100 person-years)	HR (95% CI)
			Mean ± SD	Median		
All-cause mortality	ITT	ACEI/ARB	1.61 ± 1.20	1.33	18.8	0.83 (0.75–0.92)
		Nonuser	1.54 ± 1.18	1.27	22.6	
	AT	ACEI/ARB	0.74 ± 0.82	0.46	13.4	0.61 (0.52–0.72)
		Nonuser	1.07 ± 1.02	0.75	22.6	
CV death	ITT	ACEI/ARB	1.61 ± 1.20	1.33	7.5	0.74 (0.63–0.87)
		Nonuser	1.54 ± 1.18	1.27	10.2	
	AT	ACEI/ARB	0.74 ± 0.82	0.46	5.5	0.69 (0.54–0.89)
		Nonuser	1.07 ± 1.02	0.75	8.1	

Shen et al, Nephrol Dial Transplant. April 2016:gfw053.

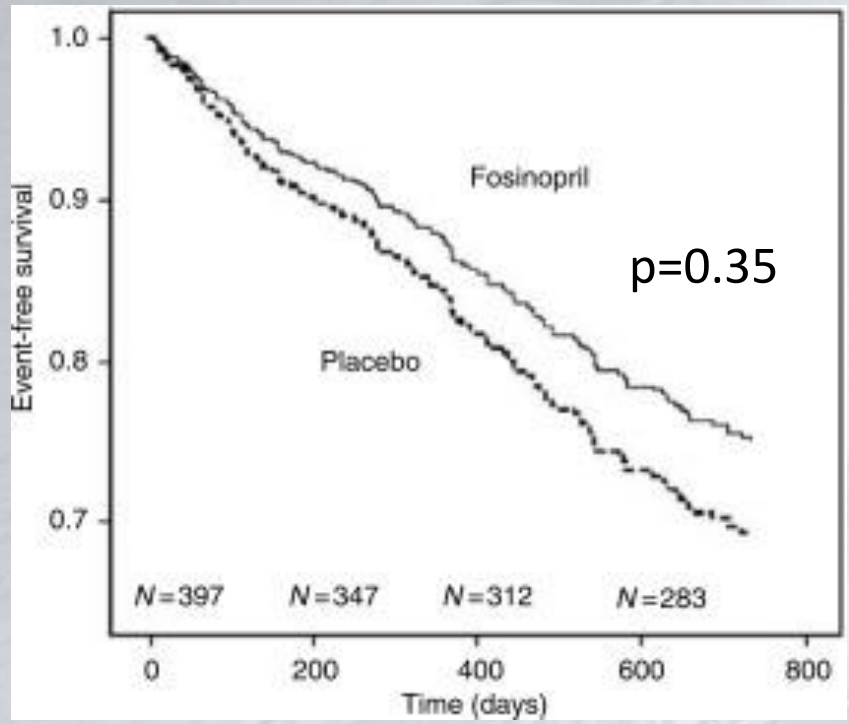
ACE inhibitors and ARBs

ACEi

- randomized trial, 397 patients with left ventricular hypertrophy (hypertension was not inclusion criteria)
- fosinopril (up to 20mg/d) vs placebo, follow-up: 48 months
- fosinopril lowered SBP
- cardiovascular events: no difference

Variable	RR	95% CI	*P*-value
Age (years)	1.02	1.00–1.05	0.052
Diabetes	1.34	0.91–1.97	0.136
Coronary artery disease	2.14	1.35–3.39	0.001
Stroke	1.64	0.94–2.87	0.08
Peripheral artery disease	2.00	1.29–3.11	0.002
LV mass[a]	24.05	6.21–93.11	0.000
Fosinopril treatment	0.93	0.68–1.26	0.35

CI, confidence interval; LV, left ventricular.
[a]Log transformed.

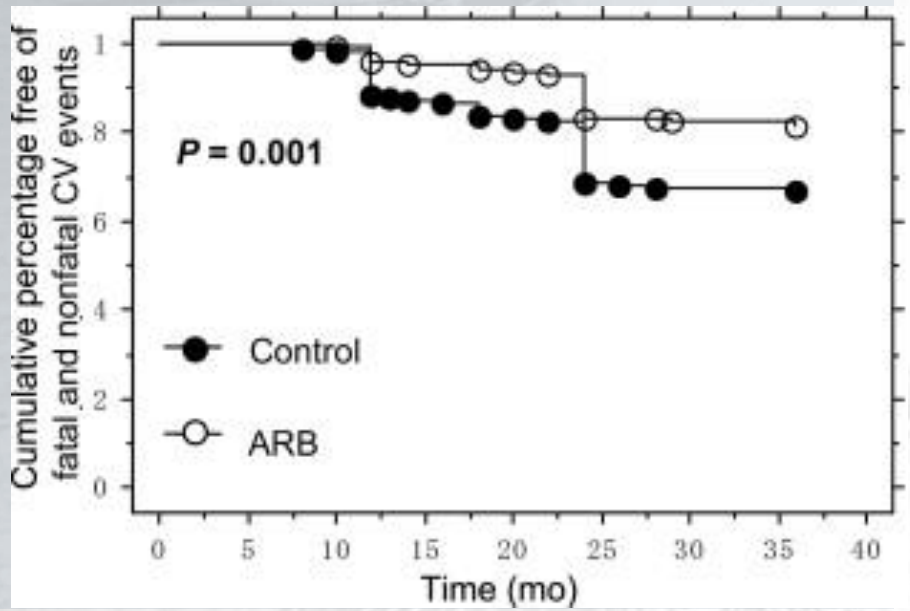


Zannad et al, Kidney Int. 2006;70(7):1318-1324.

ACE inhibitors and ARBs

ARB

- randomized trial, 360 patients with hypertension
- ARBs (candesartan, losartan, valsartan) vs other non RAAS blocker
- follow-up: 36 months
- lower incidence of cardiovascular death and events with ARBs
- 49% relative risk reduction (0.33-0.79)
  adjusted for: age, gender, diabetes, SBP, and center
- no difference in blood pressure



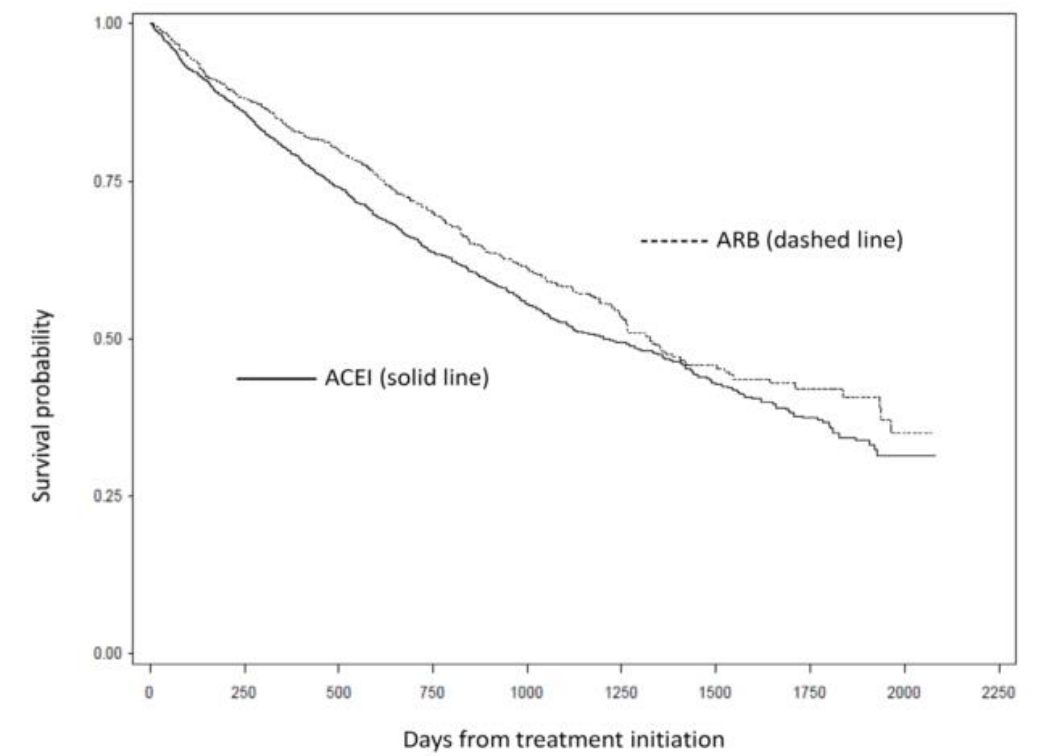
Suzuki et al, Am J Kidney Dis. 2008;52(3):501-506.

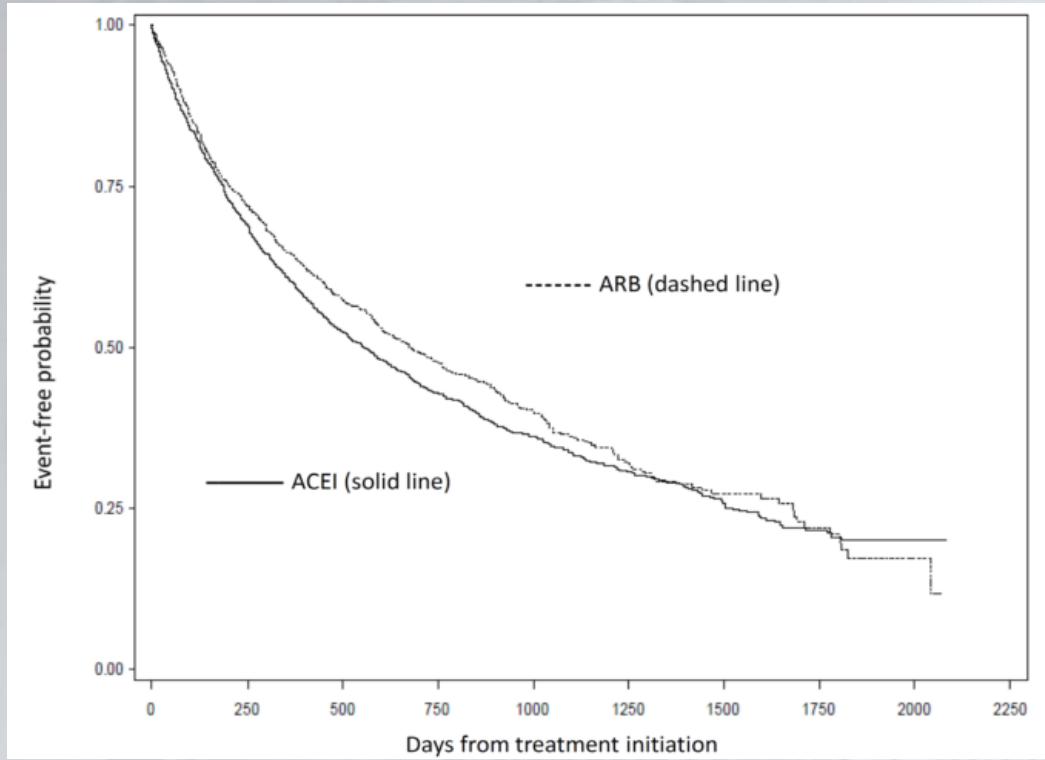
ACE inhibitors versus ARBs in patients on HD

ACEi vs. ARB

- USRDS cohort study, using "new user paradigm", n=4997 / 4635
- survival advantage with ARBs
- no difference in CV event rate

	All-cause mortality		CV-Endpoint	
	AHR	99% CI	AHR	99% CI
ACEI (1) vs. ARB (0)	1.22	1.05-1.42	1.12	0.99-1.27
Age, per 10 years	1.25	1.18-1.32	1.07	1.02-1.12
Vintage, per year	1.14	0.46-2.80	0.62	0.28-1.35
Female sex	1.08	0.94-1.25	1.17	1.04-1.32





Shireman et al, Kidney Blood Press Res. 2016;41(6):873-885.

ACE inhibitors and ARBs

- ARBs might be better in prevention of cardiovascular events and death
- ***ACE inhibitors are dialysable*** and require additional dosing after HD !
- these medications have better effect in volume contracted state

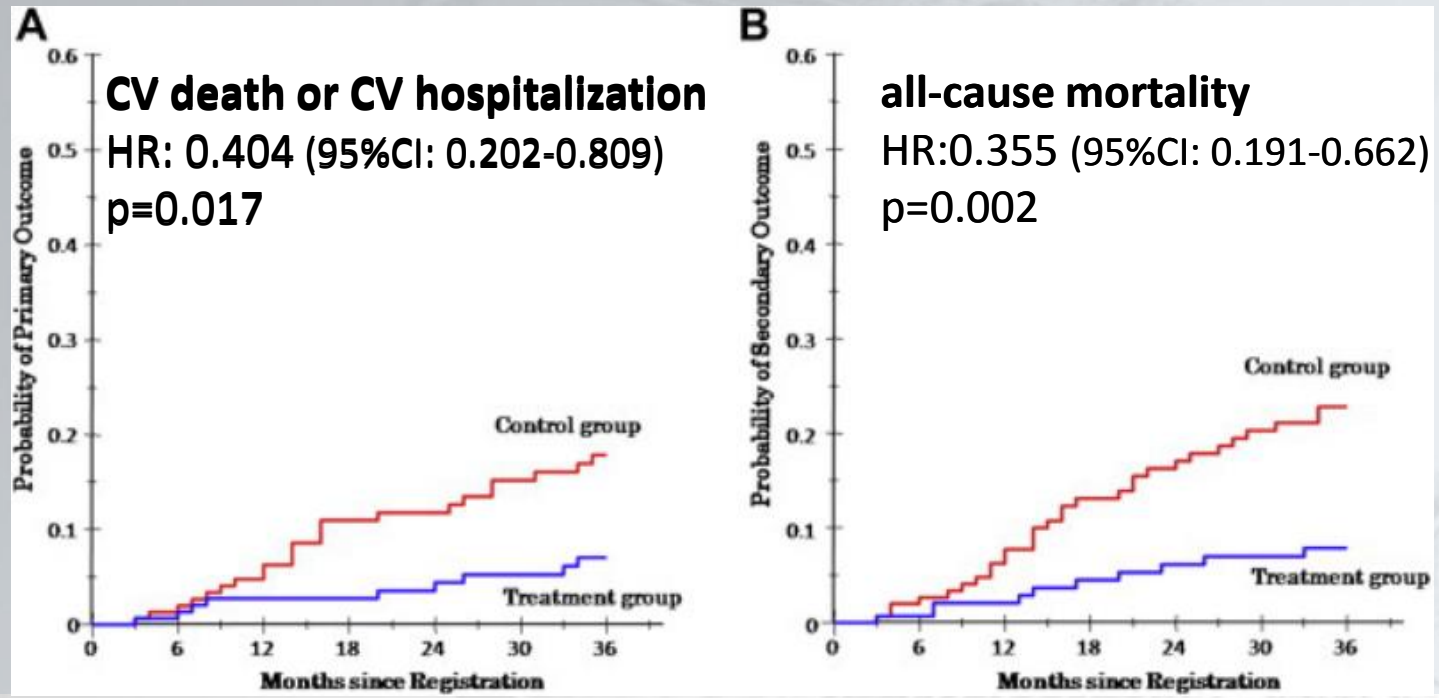
	Usual dose	Excretion	GFR < 10 ml/min	Removal with dialysis: Hemodialysis	Removal with dialysis: Peritoneal dialysis	Supplement for dialysis
ACEi						
Benazapril	5–40 mg q.d.	K (L)	50–75%	Negligible	None	5–10 mg
Captopril	12.5–50 mg t.i.d.	K	50%	50%	None	12.5–25 mg
Enalapril	2.5–10 mg q12 h	K (L)	50%	50%	None	2.5–5 mg
Fosinopril	10 mg q.d.	K (L)	75%	None	None	None
Lisinopril	2.5–10 mg q.d.	K	25–50%	50%	None	2.5–5 mg
Perindopril	2–8 mg/day	K (L)	25–50%	50%	None	2 mg
Quinapril	10–20 mg q.d.	K (L)	50%	25%	None	10 mg
Ramipril	5–10 mg q.d.	K (L)	25–50%	20%	None	2.5 mg
Trandolapril	0.5–4 mg/day	K (L)	25–50%	30%	None	0.5 mg
ARB						
Candesartan	8–35 mg/day	K (L)	100%	None	None	None
Eprosartan	600–1200 mg/day	L	100%	None	None	None
Ibersartan	75–300 mg/day	L	100%	None	None	None
Losartan	50–100 mg q.d.	K (L)	100%	None	None	None
Olmesartan	10–40 mg/day	K (L)	100%	None	None	None
Telmisartan	40–80 mg/day	L	100%	None	None	None
Valsartan	80–320 mg q.d.	L (K)	100%	None	None	None

- Clear benefit of *preserving residual kidney function (both HD & PD)*

Mineralocorticoid receptor antagonists

earlier suggestion: avidance regarding risk of hyperkalemia

- randomized trial, 309 oligo-anuric patients on hemodialysis
- spironolactone 25mg vs control, follow-up: 3 year
- **lower CV death and all-cause mortality**
- hyperkalemia: 3%
- gynecomastia: 10%

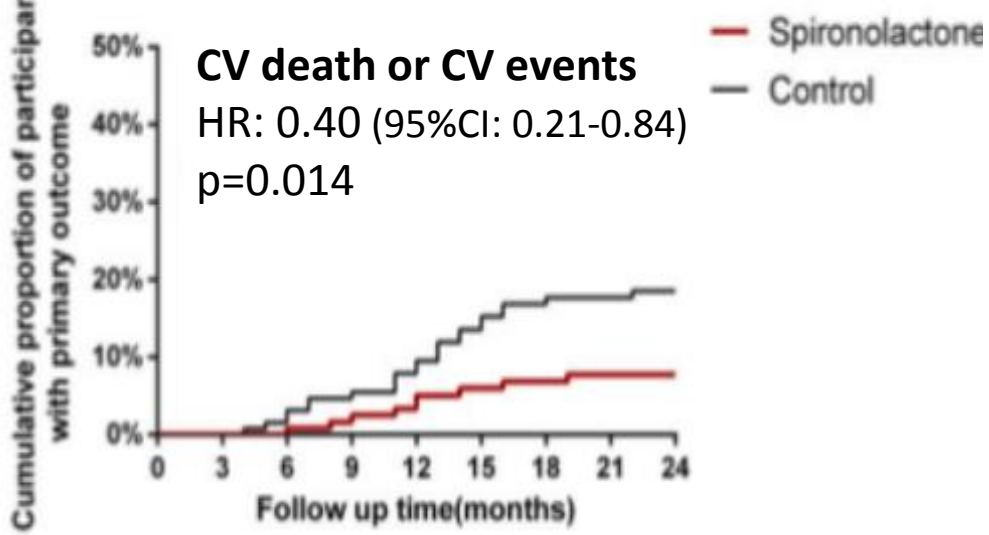


Matsumoto et al, J Am Coll Cardiol. 2014;63(6):528-536.

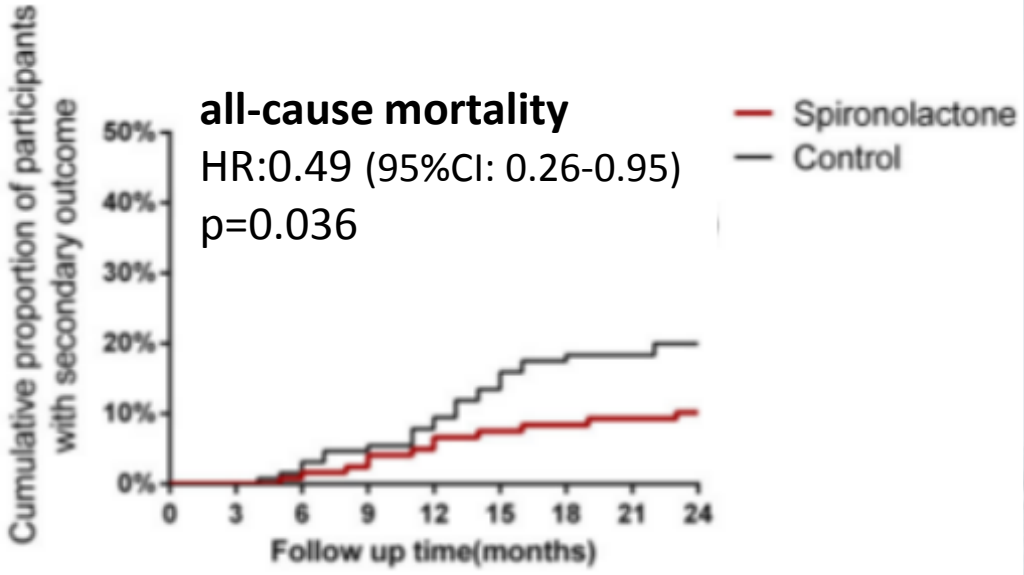
Mineralocorticoid receptor antagonists

earlier suggestion: avidance regarding risk of hyperkalemia

- randomized trial, 253 HD patients <u>without heart failure</u>
- spironolactone 25mg vs control, follow-up: 2 year
- **lower CV death and all-cause mortality**



CV death or CV events
HR: 0.40 (95%CI: 0.21-0.84)
p=0.014



all-cause mortality
HR:0.49 (95%CI: 0.26-0.95)
p=0.036

Lin et al, J Clin Hypertens. 2015;18(2):

Other agents

Alpha-adrenergic blocking agents

- safe in dialysis patients, avoid if intradialytic hypotension
- no additional dosing after HD required
- risks: <u>orthostatic hypotension</u>

•Direct vasodilators

- effective and safe in dialysis
- hydralazin and minoxidil are not dialysable

•Central acting sympatholytics

- rarely used due to side effects

Fears, Beliefs and Facts

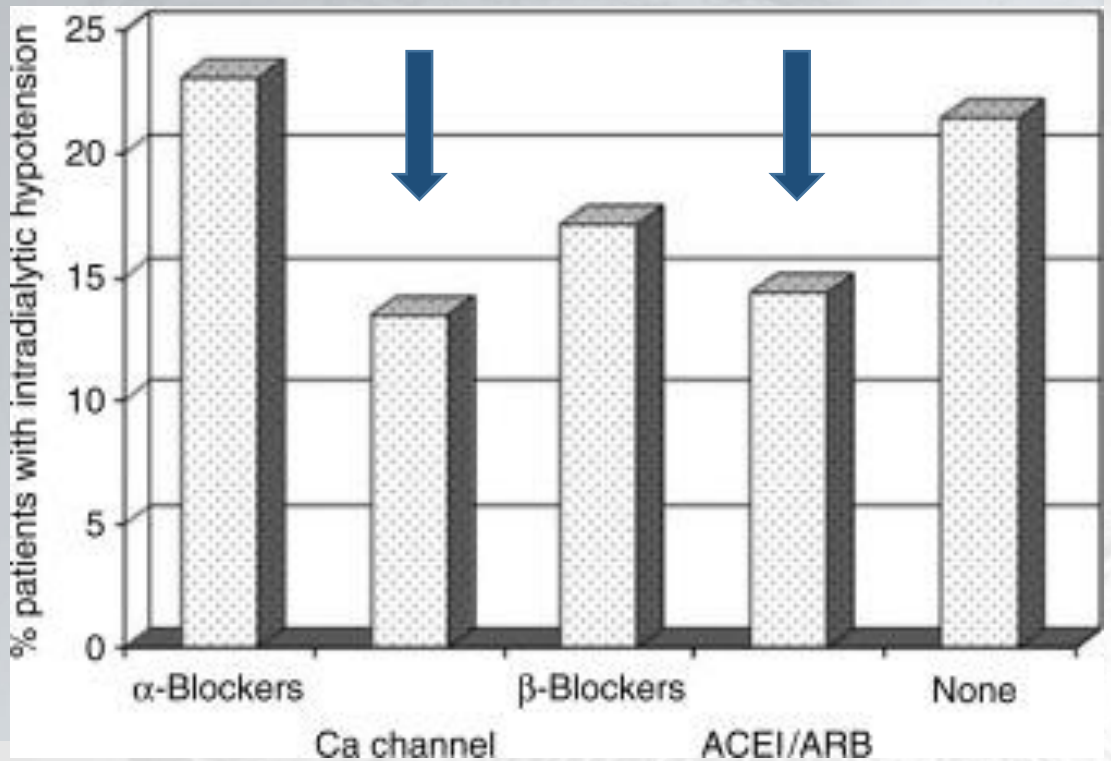
- 57% of patients are advised no to take medication before dialysis
  - "Meds are removed during HD - useless to take"
    - very few meds are removed (ACE inhibitors, few beta blockers)
  - "Intradialytic hypotension caused by antihypertensives"
    - not proven
    - mainly <u>if antihypertensive therapy is driven by pre-dial BP !</u>

Davenport et al, Kidney International 2008; 73 (6): 759–764

Antihypertensives and intradialytic hypotension

- 2630 prevalent HD patients in Greater London area
- Incidence of intradialytic hypotension
  - without antihypertensive therapy: 21%
  - with antihypertensive therapy: 13% !! ($p<0.001$)

<u>no significant association between drug prescription and hypotensive events</u>



Davenport et al, Kidney International 2008; 73 (6): 759–764

Fears, Beliefs and Facts

- 57% of patients are advised no to take medication before dialysis
  - "Meds are removed during HD - useless to take"
    - very few meds are removed (ACE inhibitors, few beta blockers)
  - "Intradialytic hypotension caused by antihypertensives"
    - not proven
    - mainly <u>if antihypertensive therapy is driven by pre-dial BP !</u>
- <u>orthostatic hypotension</u>
  - falls and fractures, cognitive decline

  if therapy prescribed for normotensive patients

  <u>Don't treat pre-dialysis blood pressure!</u>

Davenport et al, Kidney International 2008; 73 (6): 759–764

Summary & recommendations

1. Encourage patients to measure BP at home (BP diary)
2. Diagnose hypertension based on home BP monitoring / ABPM
3. Start with optimal dry-weight reduction and salt restriction
   - carefully lower dialysate Na ?
4. Combination medical therapy with
   - beta-blockers, Ca-channel blockers, RAAS inhibitors

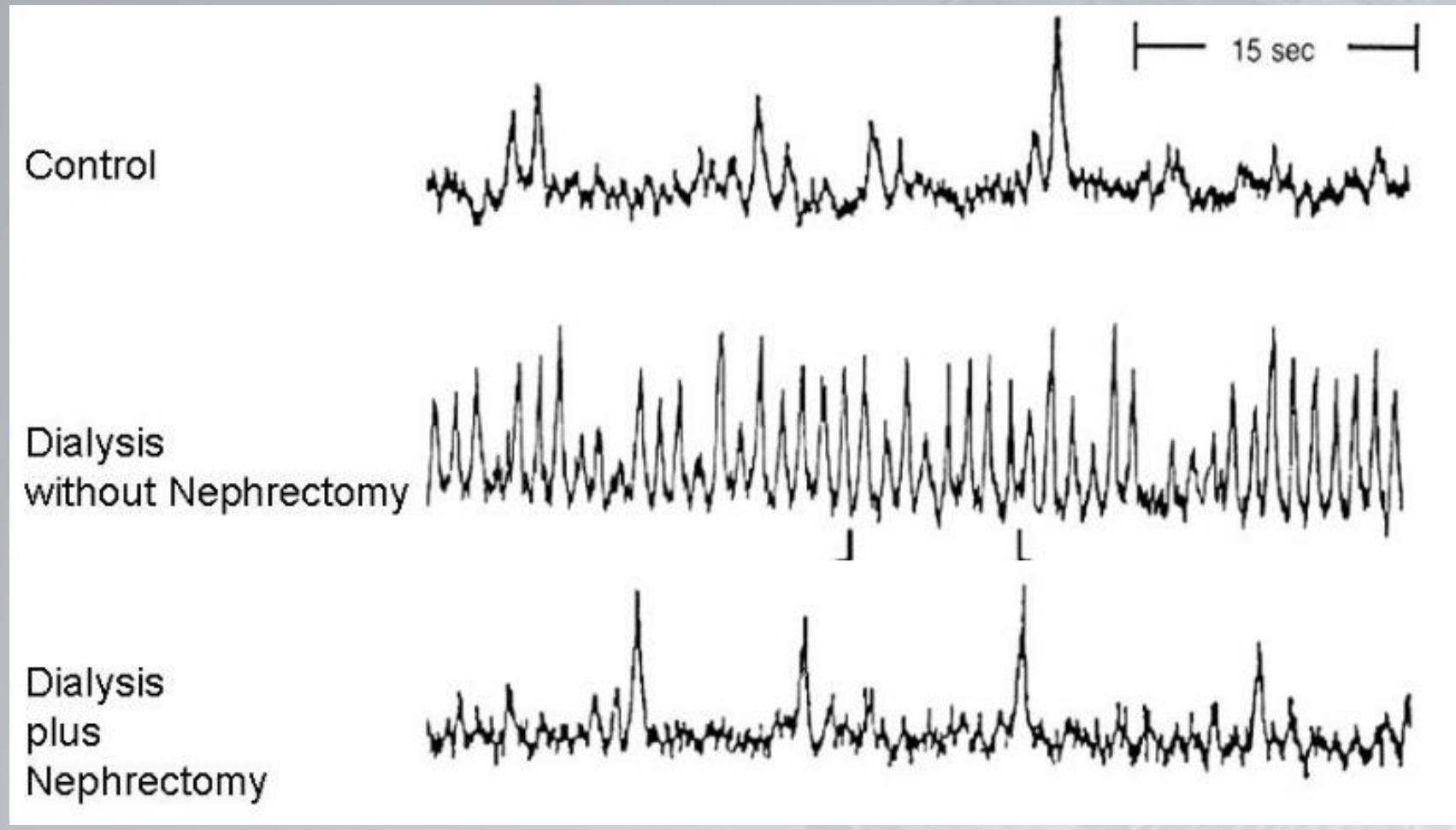
5. Do not forget about secondary causes of hypertension !

What is the *optimal blood pressure target* in dialysis patients?

Thank you.

Sympathetic overactivity in dialysis

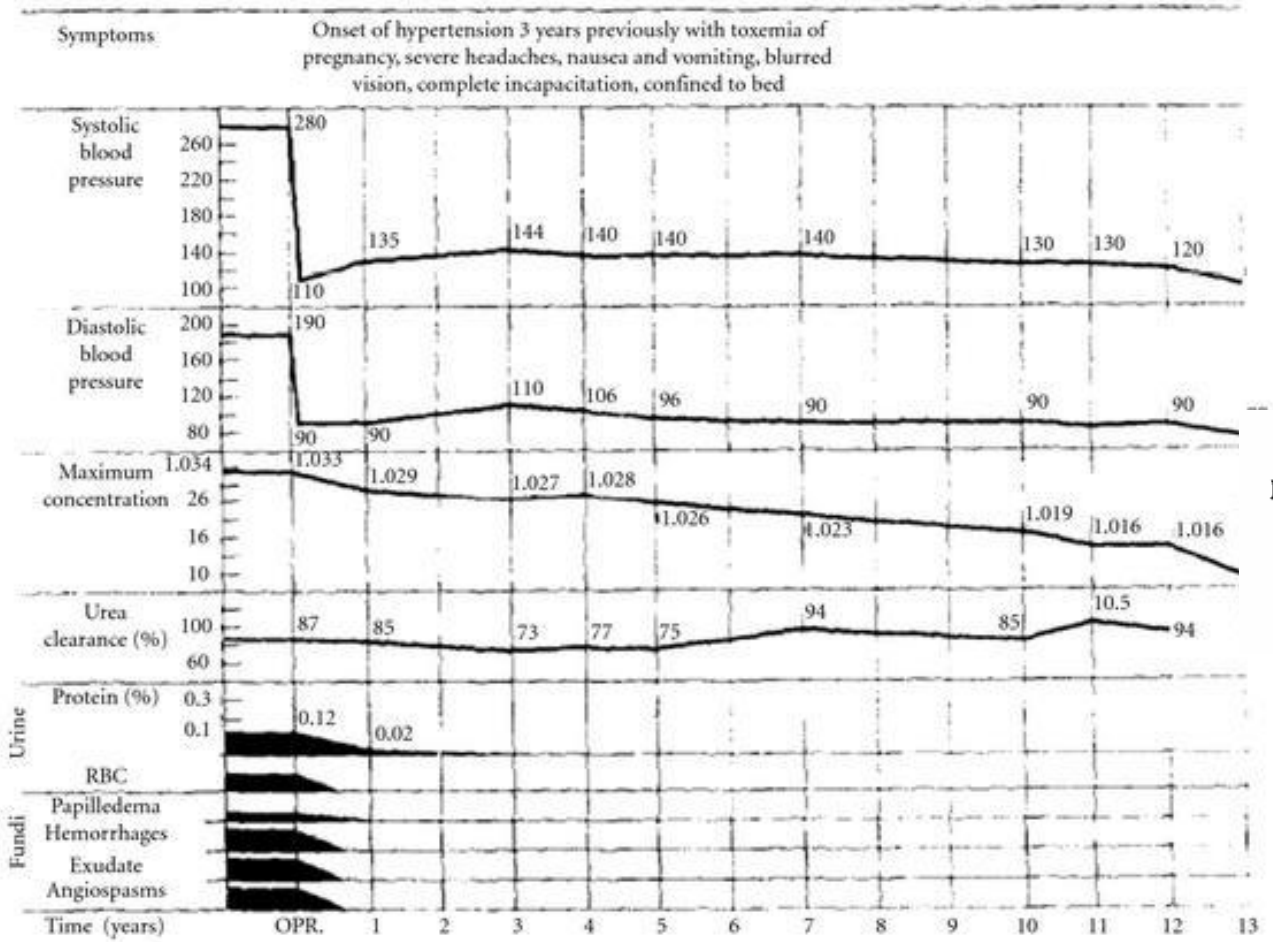
- Patients on hemodialysis, before and after bilateral nephrectomy



Chris et al, Br Med Journal 1951; 1(4708): 665-670
Augustyniak et al, J Hypertens 2002; 20(1): 3-9

Sympathetic overactivity in dialysis

- Surgical sympathectomy was a very effctive treatment



THE JOURNAL

of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 152, NO. 16 — CHICAGO, ILLINOIS — AUGUST 15, 1953

COPYRIGHT, 1953, BY AMERICAN MEDICAL ASSOCIATION

SPLANCHNICECTOMY FOR ESSENTIAL HYPERTENSION

RESULTS IN 1,266 CASES

Reginald H. Smithwick, M.D.
and
Jesse E. Thompson, M.D., Boston

DENERVATION OF THE KIDNEY

Hunterian Lecture delivered at the Royal College of Surgeons of England on 9th March, 1950 by J. B. Oldham, V.R.D., F.R.C.S.

A SURGICAL TREATMENT OF ESSENTIAL HYPERTENSION

BY IRVINE H. PAGE AND GEORGE J. HEUER

(From the Hospital of the Rockefeller Institute for Medical Research, and the Surgical Department, New York Hospital and Cornell Medical College, New York)

(Received for publication August 3, 1934)

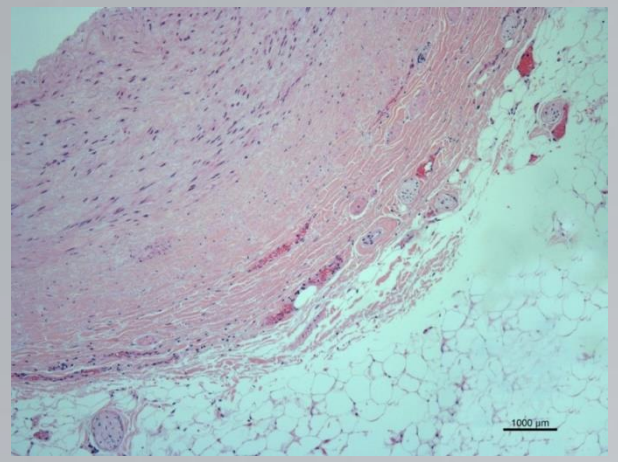
Chris et al, Br Med Journal 1951; 1(4708): 665-670

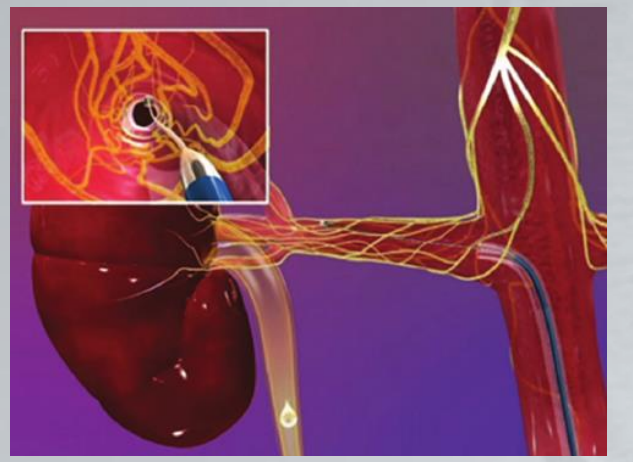
Sympathetic overactivity and the kidney

- The kidney is source of sympathetic overactivity

central sympathetic activity

- Destroying perivascular renal nerves can decrease sympathetic activity and blood pressure

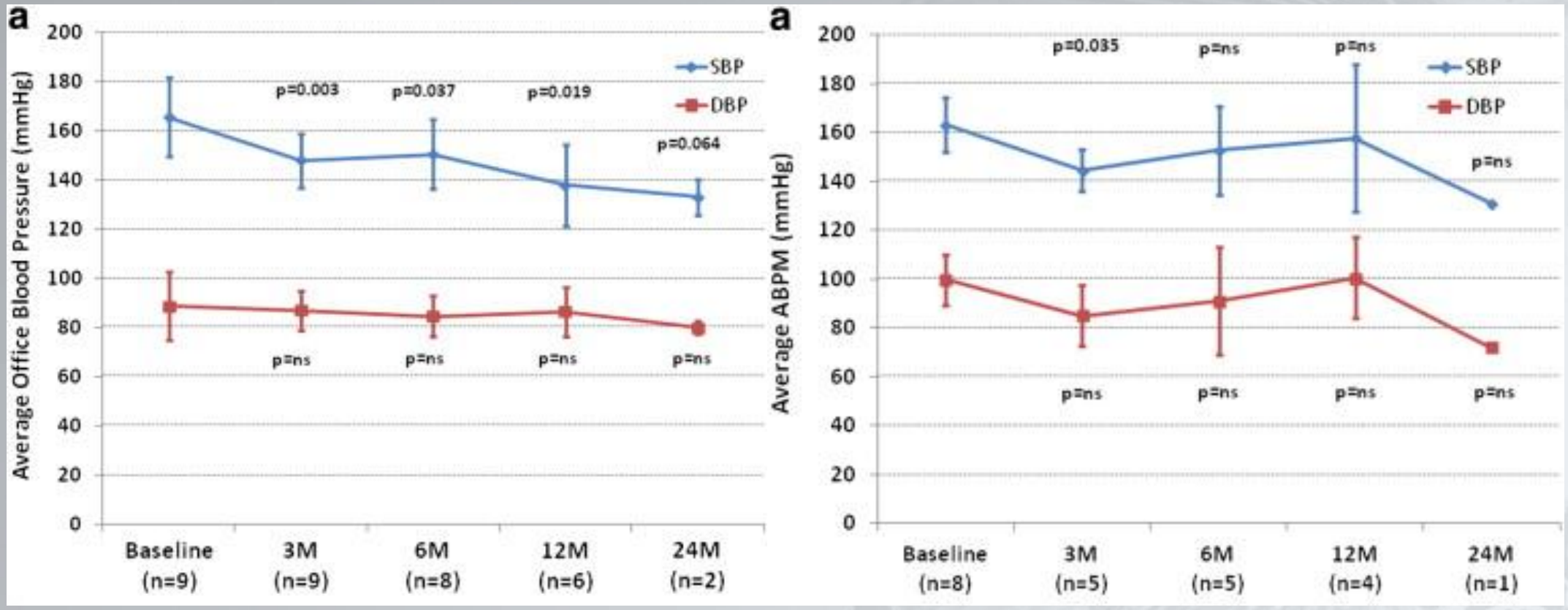




Chemoreceptors - interstitial ischaemia
+ markedly decreased renalase activity

Renal denervation in dialysis

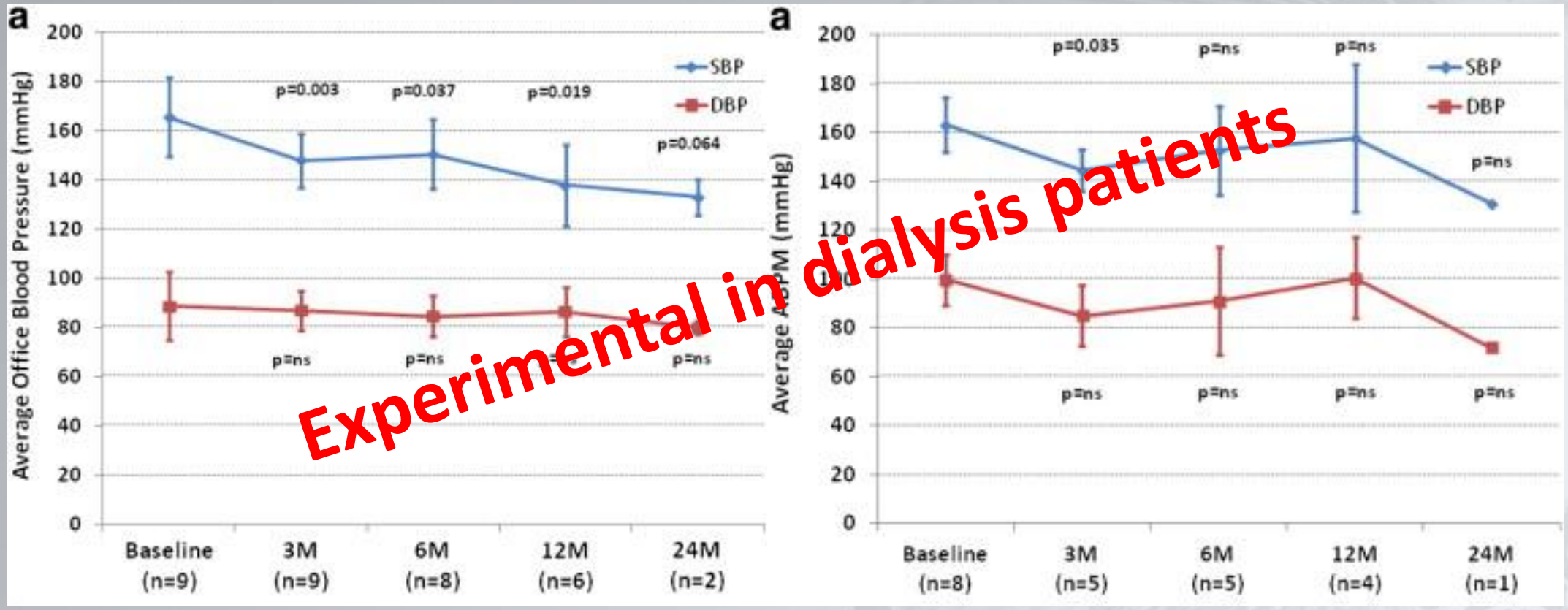
- Increasing number of case reports in dialysis patients
- Case series of 12 anuric patients on HD



Schlaich et al, Int J Cardiol. 2013;168(3):2214-2220.

Renal denervation in dialysis

- Increasing number of case reports in dialysis patients
- Case series of 12 anuric patients on HD



Experimental in dialysis patients

Schlaich et al, Int J Cardiol. 2013;168(3):2214-2220.