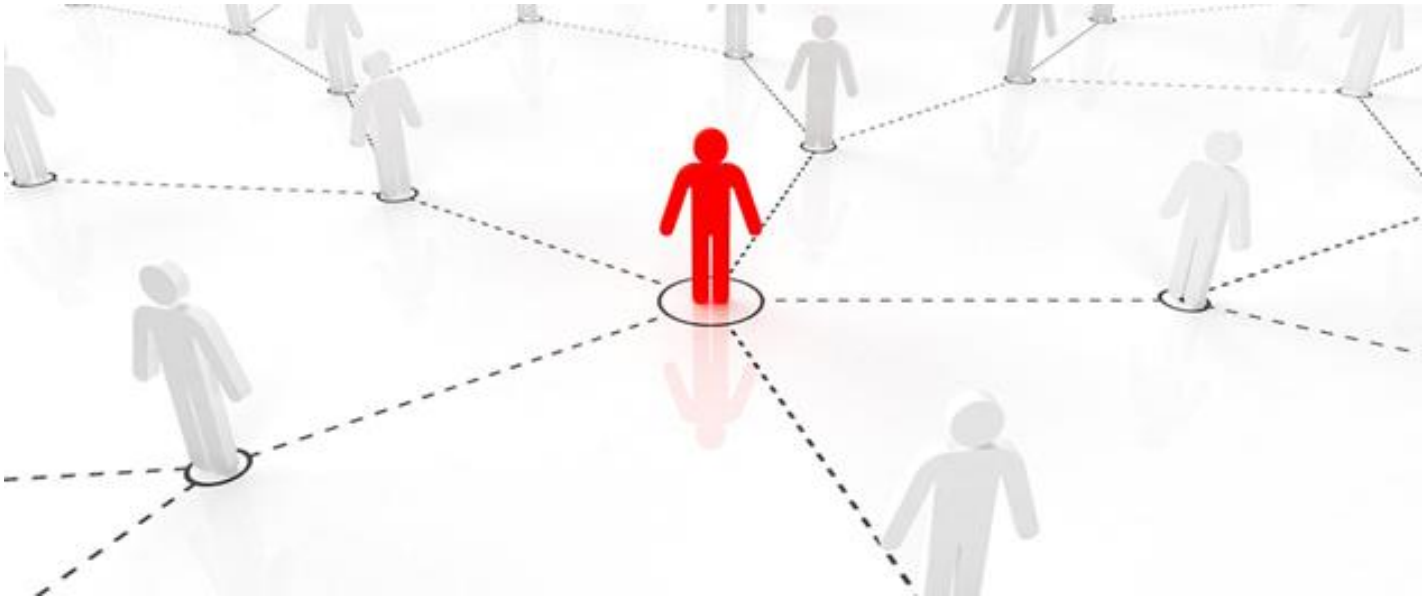
Hypertension in ESRD

Vaios Vasileios, MD, PhD

Nephrologist,
2nd Department of Nephrology, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece

1) Epidemiology

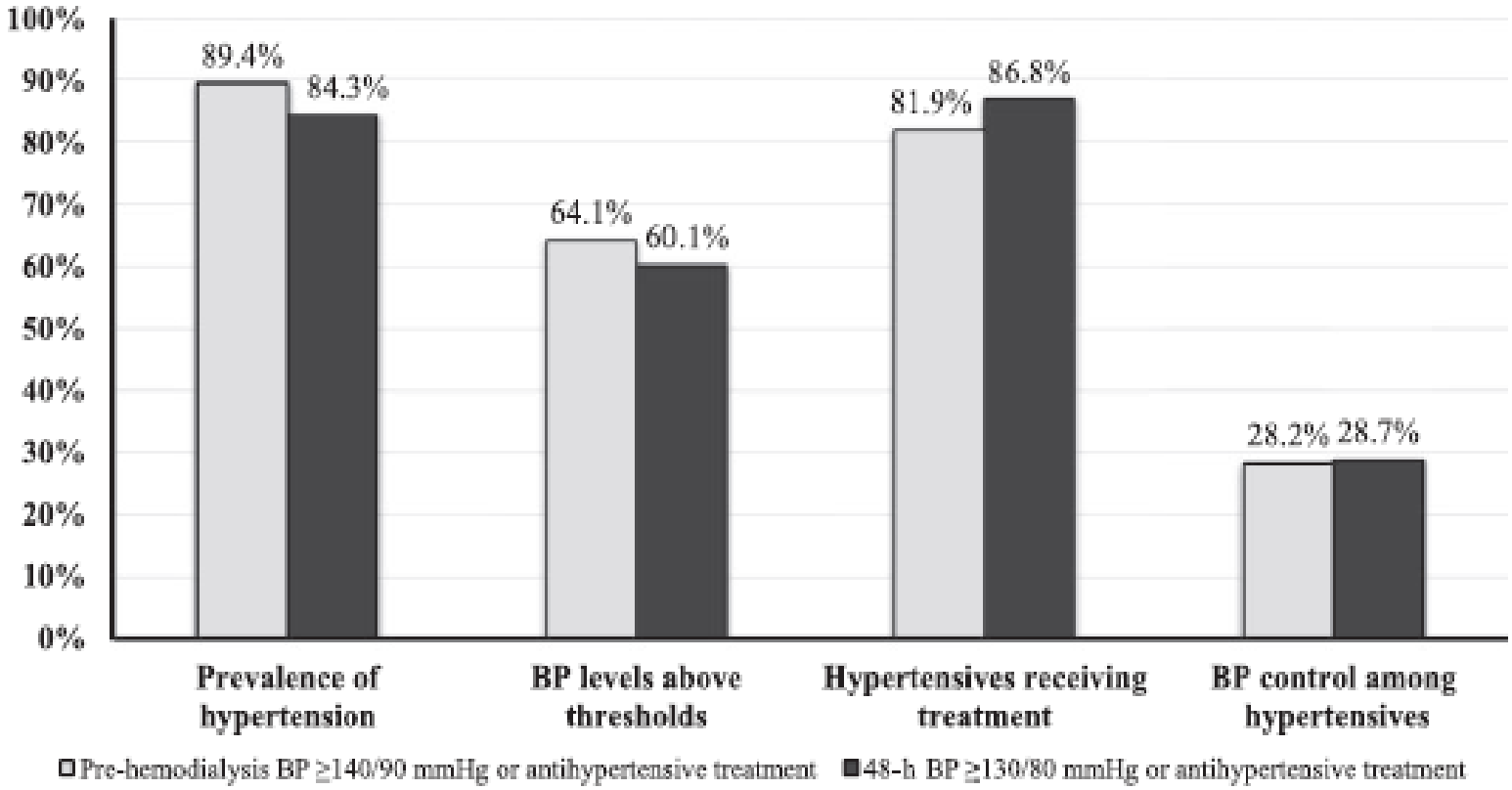


Prevalence, treatment and control of hypertension in HD patients

Author	Year	N	Definition of hypertension	Prevalence of hypertension (%)	BP treatment among hypertensives (%)	BP control among hypertensives (%)
Salem [55]	1995	649	Pre-haemodialysis MAP ≥114 mmHg or use of antihypertensive agents	71.9	81.5	48.6
Rahman *et al.* [60]	1999	489	Pre-haemodialysis SBP ≥140 mmHg and/or DBP ≥90 mm	87.7	93.2	71.1
Agarwal *et al.* [1]	2003	2535	1-week average pre-haemodialysis 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

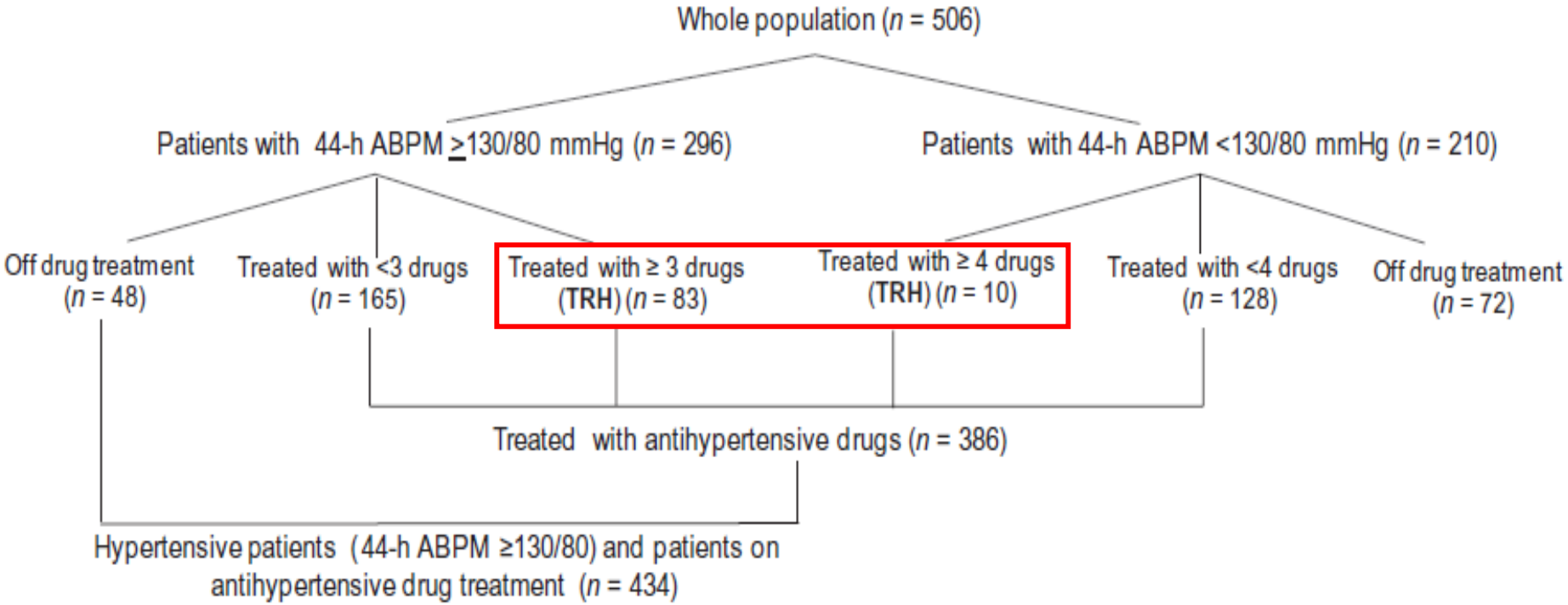
Sarafidis PA, et al. Nephrol Dial Transplant 2017;32:620-640.

Prevalence and control of hypertension by 48-h ambulatory blood pressure monitoring in haemodialysis patients: a study by the European Cardiovascular and Renal Medicine (EURECA-m) working group of the ERA-EDTA



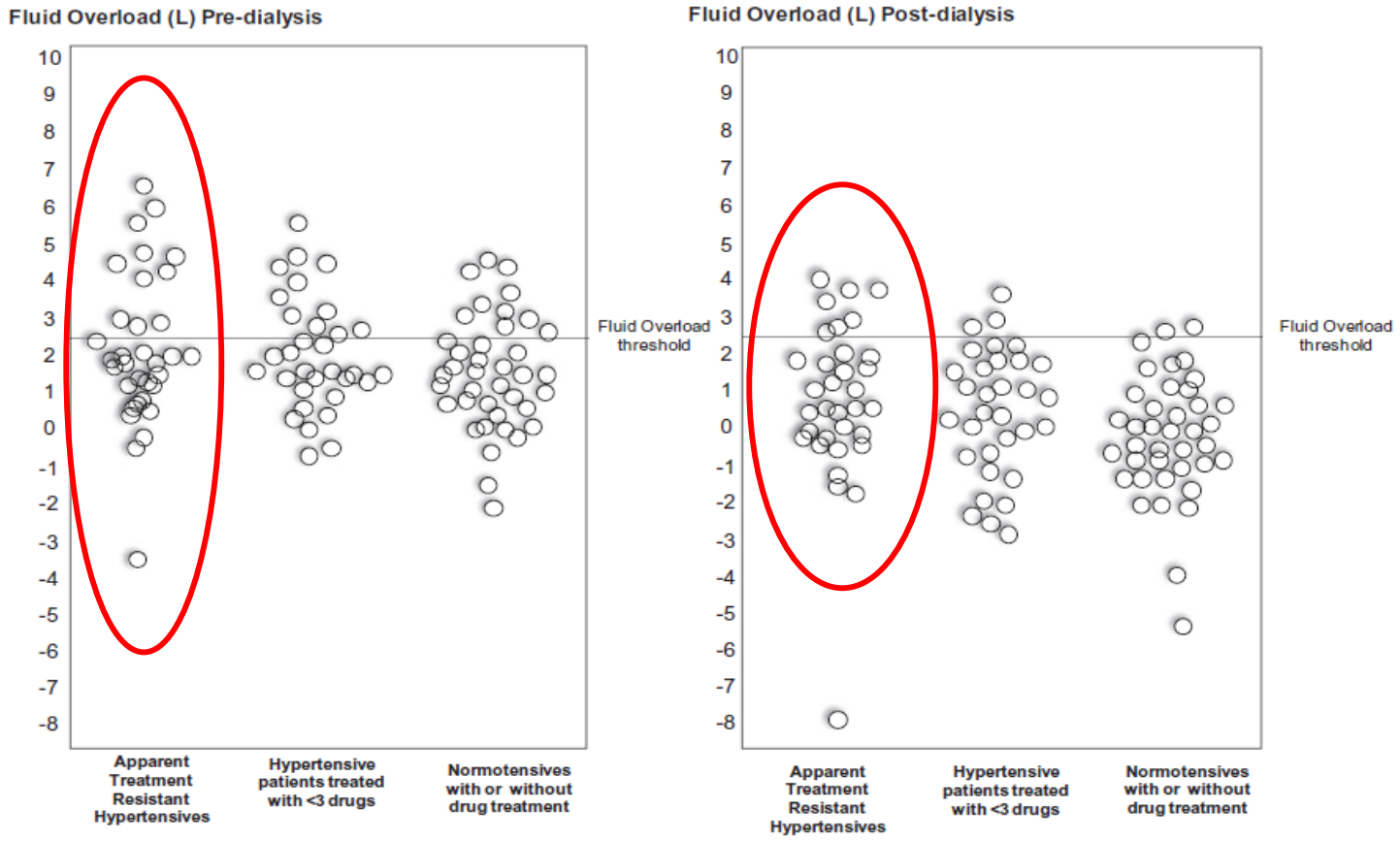
Sarafidis PA, et al. Nephrol Dial Transplant 2019; 34: 1542-48.

Treatment-resistant hypertension in the hemodialysis population: a 44-h ambulatory blood pressure monitoring-based study



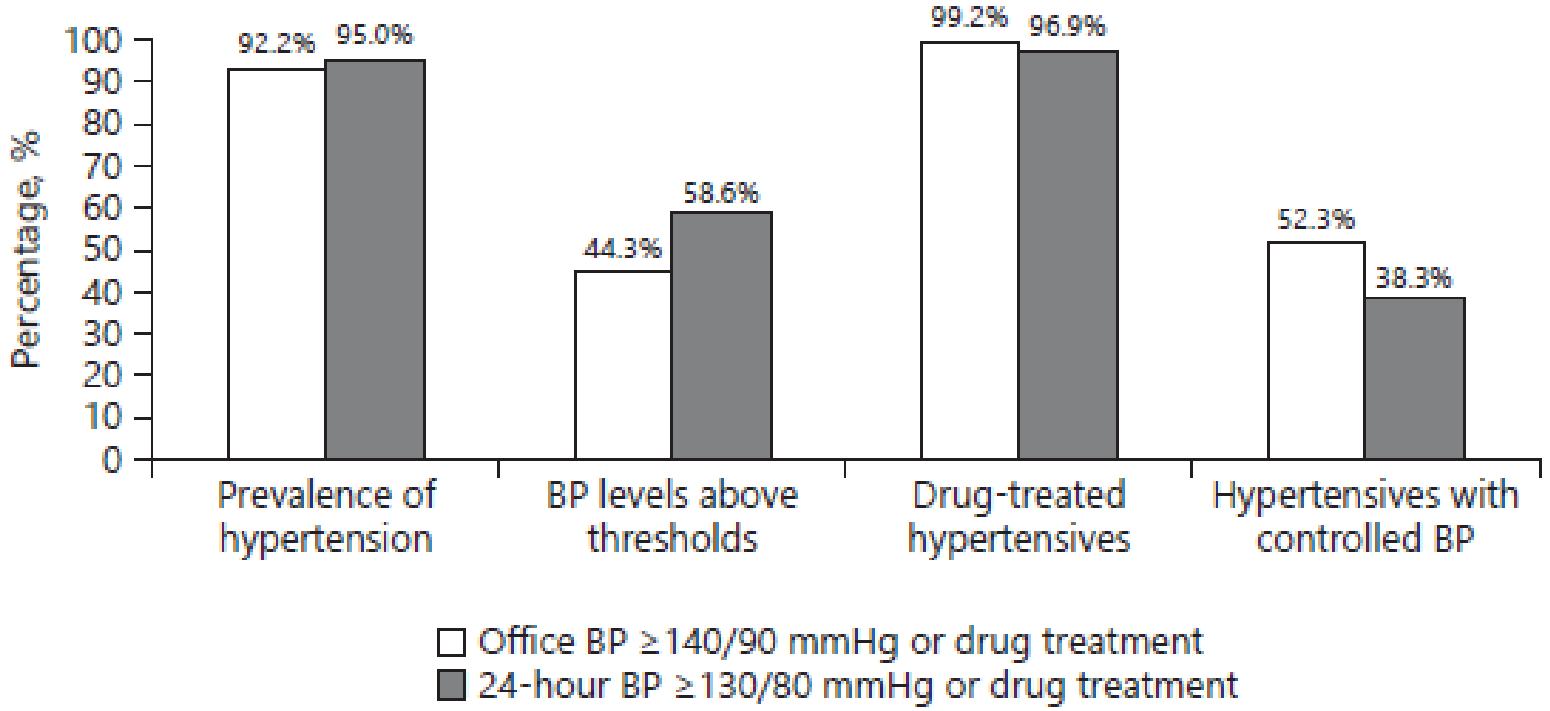
Mallamaci F, et al. J Hypertens 2020; 38: 1849-56.

Treatment-resistant hypertension in the hemodialysis population: a 44-h ambulatory blood pressure monitoring-based study



Mallamaci F, et al. J Hypertens 2020; 38: 1849-56.

Epidemiology of Hypertension among Patients on Peritoneal Dialysis Using Standardized Office and Ambulatory Blood Pressure Recordings



Vareta G, Georgianos P, Vaios V, Liakopoulos V. Am J Nephrol.2022;53(2-3):139-147

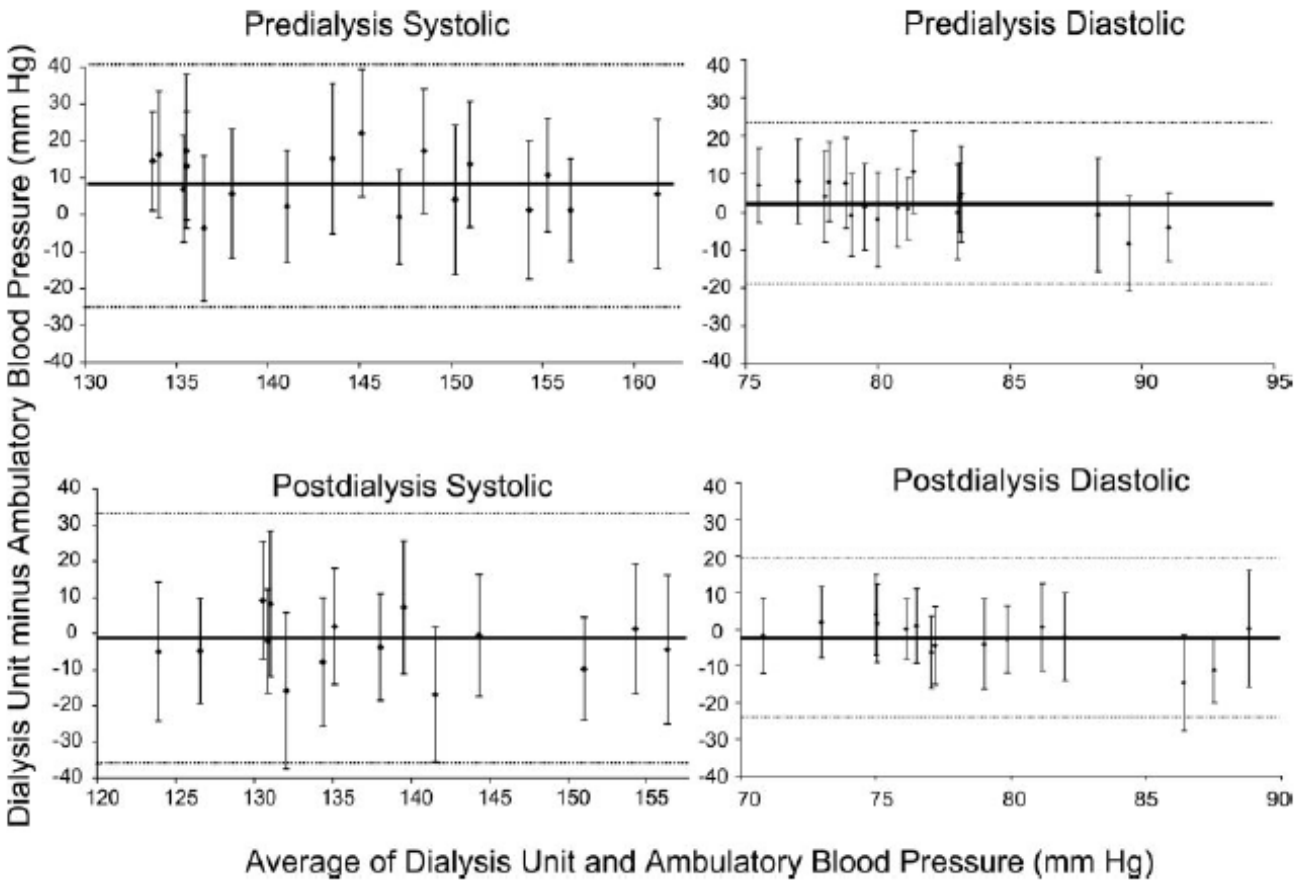
Epidemiology of Hypertension among Patients on Peritoneal Dialysis Using Standardized Office and Ambulatory Blood Pressure Recordings

Parameter	Univariate analysis			Multivariate analysis		
	crude OR	95% CI	*p* value	adjusted OR	95% CI	*p* value
Age (per year higher)	0.841	0.660–1.071	0.16	1.000	0.734–1.361	0.99
Male gender	0.977	0.474–2.011	0.95			
BMI (per kg/m^2 higher)	0.994	0.921–1.072	0.87			
PD vintage (≥24 vs. <24 months)	0.513	0.251–1.048	0.07	0.391	0.144–1.062	0.07
PD modality (continuous ambulatory vs. automated)	0.404	0.198–0.827	<0.05	0.978	0.374–2.556	0.96
Peritoneal transport status			0.14			0.33
Low	Reference category			Reference category		
Low-average	1.094	0.299–4.006	0.89	1.129	0.249–5.109	0.88
High-average	2.435	0.735–8.071	0.15	2.165	0.544–8.620	0.27
High	3.033	0.676–13.607	0.15	3.805	0.675–21.411	0.13
History of cardiovascular disease (yes vs. no)	3.022	1.461–6.252	<0.01	3.069	1.157–8.140	0.02
History of diabetes (yes vs. no)	0.892	0.436–1.822	0.75			
Current smoker (yes vs. no)	0.332	0.116–0.949	<0.05	0.331	0.093–1.183	0.09
Overhydration (per L higher)	1.201	0.982–1.469	0.07	1.308	1.023–1.673	0.03
Antihypertensive medications (per 1 drug higher)	1.419	0.963–2.093	0.08	1.003	0.640–1.574	0.99
Residual diuresis >0.5 L/24 h (yes vs. no)	0.572	0.258–1.269	0.17	0.304	0.105–0.881	0.03
Hemoglobin (per g/dL higher)	0.854	0.679–1.074	0.18	1.068	0.804–1.418	0.65
Serum albumin (per g/dL higher)	1.253	0.494–3.177	0.64			
Epoetin use (yes vs. no)	0.543	0.263–1.123	0.10	0.506	0.197–1.296	0.16
Statin use (yes vs. no)	0.613	0.282–1.332	0.22			

Vareta G, Georgianos P, Vaios V, Liakopoulos V. Am J Nephrol.2022;53(2-3):139-147

2) Diagnosis

Pre- and Postdialysis Blood Pressures Are Imprecise Estimates of Interdialytic Ambulatory Blood Pressure



Agarwal R, et al. Clin J Am Soc Nephrol 2006;1(3):389-98.

Out-of-Hemodialysis-Unit Blood Pressure Is a Superior Determinant of Left Ventricular Hypertrophy

B: Regression Analysis When Complete Data Were Available on All BP (n=97)						
Statistic	2-Week Averaged Routine BP		2-Week Averaged Standardized BP		1-Week Averaged Home BP	44-h Ambulatory BP
	Pre-HD	Post-HD	Pre-HD	Post-HD		
Slope	0.090±0.071	0.102±0.077	0.089±0.067	0.107±0.072	0.212±0.067	0.149±0.071
Intercept	44.5±10.4	44.2±10.2	45.2±9.4	44.8±8.8	28.0±9.5	38.6±9.2
r^2	0.017	0.018	0.018	0.022	0.095	0.044
P	0.206	0.188	0.188	0.14	0.002	0.039
F	1.6	1.8	1.8	2.2	9.9	4.4
SEE	14.7	14.7	14.7	14.7	14.1	14.5
*r^2 is the coefficient of determination, P the significance level, F is the ratio of regression mean square to error mean square, and SEE is the standard error of regression estimate.						

Agarwal R et al. Hypertension. 2006 Jan;47(1):62-8

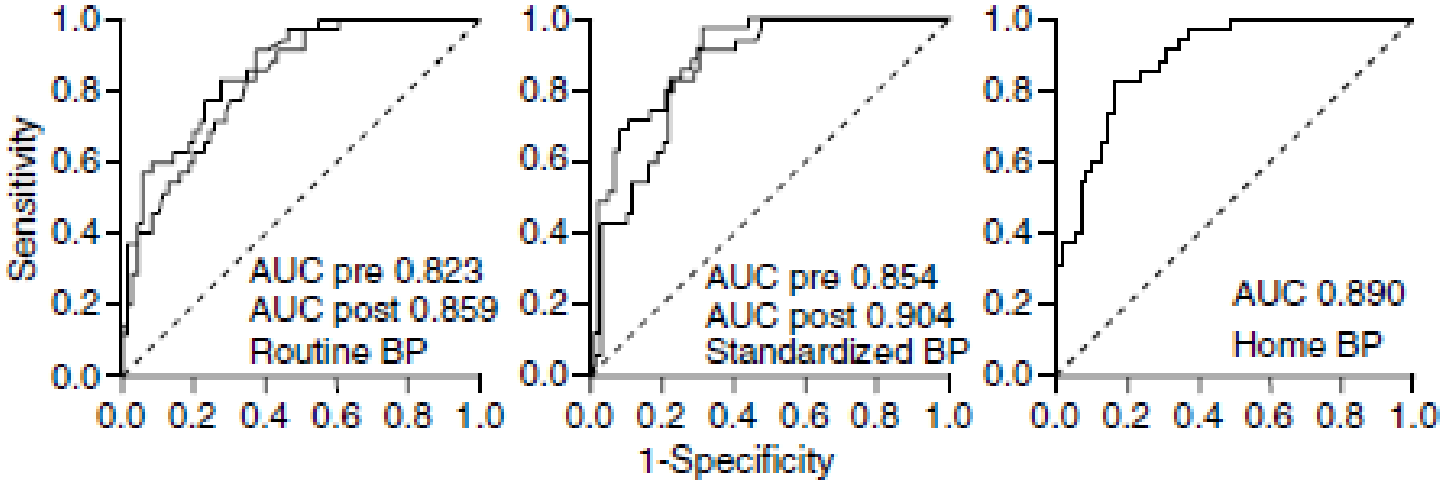
Diagnosing Hypertension by Intradialytic Blood Pressure Recordings

Table 3. Bias, precision, and accuracy of dialysis unit BP measurements

Method No.	Timing	44 h-Systolic Ambulatory BP − Systolic BP (mmHg)				44 h-Diastolic Ambulatory BP − Diastolic BP (mmHg)			
		Mean Difference Systolic BP	95% CI of Difference	SD of Difference	Accuracy	Mean Difference Diastolic BP	95% CI of Difference	SD of Difference	Accuracy
1	Pre-HD	−16.9	−19.9, −13.8	17.8	24.5	−6.2	8.0, −4.4	10.7	12.4
2	Post-HD	−4.0	−6.9, −1.1	17.2	17.7	0.1	−1.7, 1.9	10.6	10.6
3	Intradialytic	−5.4	−8.0, −2.8	15.2	16.1	−0.9	−2.6, 0.8	10.0	10.0
4	Intradialytic + pre-HD + post-HD	−6.4	−8.9, −3.9	14.7	16.0	−1.3	−3.0, 0.3	9.7	9.8
5	Pre-HD + post-HD	−10.6	−13.1, −8.0	15.0	18.4	−3.1	−4.7, −1.4	9.7	10.2

Agarwal R, et al. Clin J Am Soc Nephrol 2008;3:1364-1372

Home blood pressure monitoring improves the diagnosis of hypertension in hemodialysis patients

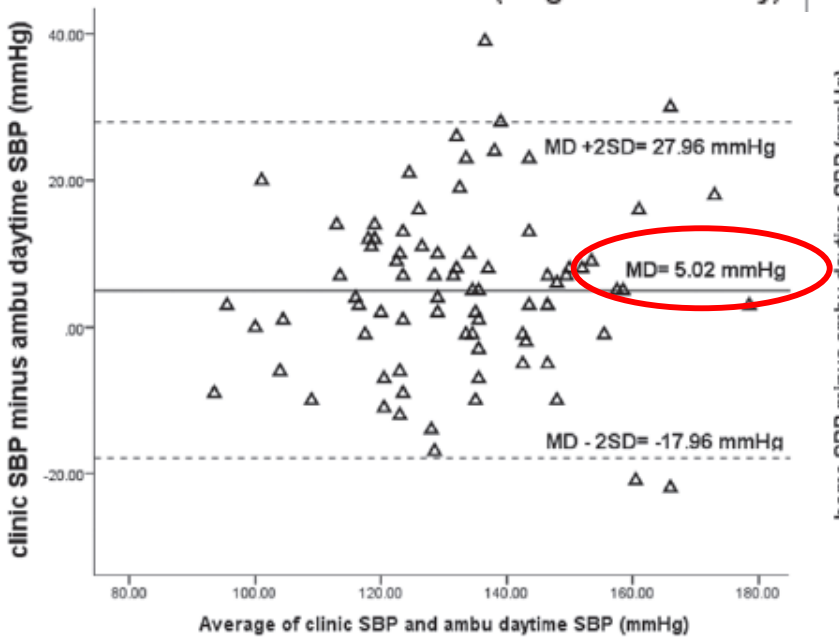


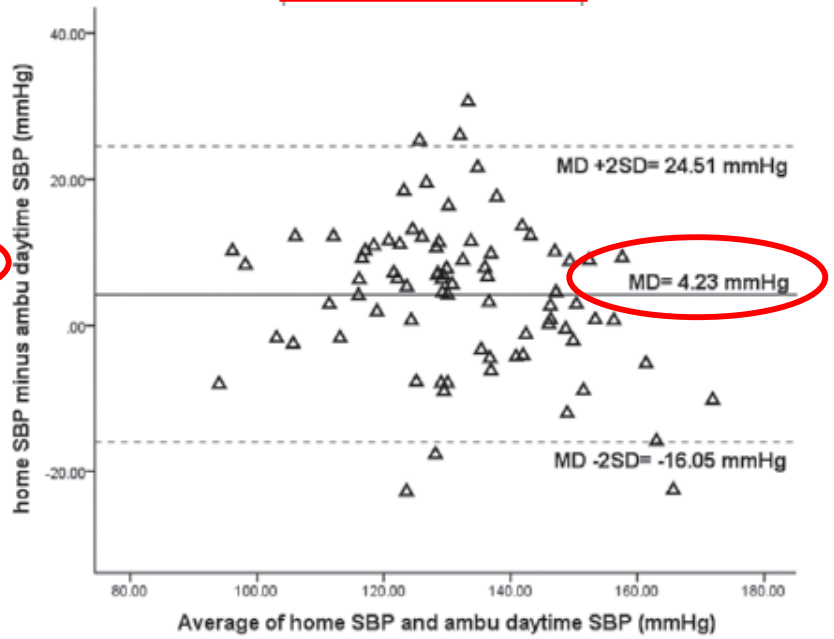
	Two-week averaged routine BP		Two-week averaged standardized BP		
	Pre-HD	Post-HD	Pre-HD	Post-HD	One-week averaged home BP
Area under ROC curve (95% CI)	0.823 (0.744-0.902)	0.859 (0.789-0.929)	0.854 (0.783-0.924)	0.904 (0.849-0.960)	0.890 (0.829-0.950)
Youden index (diagnostic efficiency)	0.509	0.553	0.610	0.667	0.669
BP threshold	145.3	130.0	143.3	114.9	148.9
Sensitivity	86.7	82.8	91.4	97.1	82.9
Specificity	65.2	72.5	69.6	69.6	84.1

Agarwal R, et al. Kidney Int 2006; 69(5):900-6.

Clinic and Home Blood Pressure Monitoring for the Detection of Ambulatory Hypertension Among Patients on Peritoneal Dialysis

Parameter	Clinic Systolic BP	Home Systolic BP
Area under ROC curve, 95% CI	0.859 (0.776–0.941)	0.895 (0.815–0.976)
Youden index (diagnostic efficacy)	0.614	0.655





Vaios V, Georgianos PI, Vareta G, Liakopoulos V et al. Hypertension 2019; 74: 998-1004

HBPM in RCTs in HD patients

Study	Design	Patients	Intervention	Follow-up	HBPM scheme	Findings
da Silva et al[4] (2009)	Open-label RCT	65 hypertensive HD patients	Home BP– vs predialysis BP–guided therapy	6 mo	HBPM 2×/d for 7 d on a monthly basis	24-h ambulatory BP decreased from 144/83 to 135/76 mm Hg in the HBPM group but was unchanged in the control group
Agarwal et al[5,6] (2009)	Open-label RCT	150 hypertensive HD patients	Dry-weight probing vs no intervention on dry weight	2 mo	HBPM 3×/d for 7 d on 3 occasions at 4-wk intervals	Home BP guided the management of dry weight and was more sensitive than pre- and postdialysis BP to track changes in 44-h ambulatory BP evoked by dry-weight reduction
Agarwal et al[7] (2014)	Open-label RCT	200 hypertensive HD patients with LVH	Atenolol (25-100 mg) vs lisinopril (10-40 mg) 3×/wk postdialysis	12 mo	HBPM 2×/d for 4 d after the midweek dialysis on a monthly basis	Home BP-guided titration of antihypertensive therapy targeting to lower home SBP < 140 mm Hg
Miskulin et al[10] (2018)	Open-label RCT	126 hypertensive HD patients	Intensive (110-140 mm Hg) vs standardized (155-165 mm Hg) predialysis SBP target	12 mo	HBPM 2× on the day after midweek dialysis, weekly thereafter	HBPM was an optional assessment and not used to guide therapy; proportion of patients with ≥1 home BP measurement: 82%, 73%, 68%, and 62% at mo 1, 4, 8, and 12, respectively
Bansal[1] (2020)	Open-label RCT	50 HD patients	Home BP– vs predialysis BP–guided therapy	4 mo	HBPM 2× on midweek nondialysis day every 2 wk	Proportion of study visits with ≥2 home BP measurements transmitted to research team was 94% during follow-up

Georgianos PI & Agarwal R. Am J Kidney Dis 2021; 77:4-6.

3) Blood pressure targets

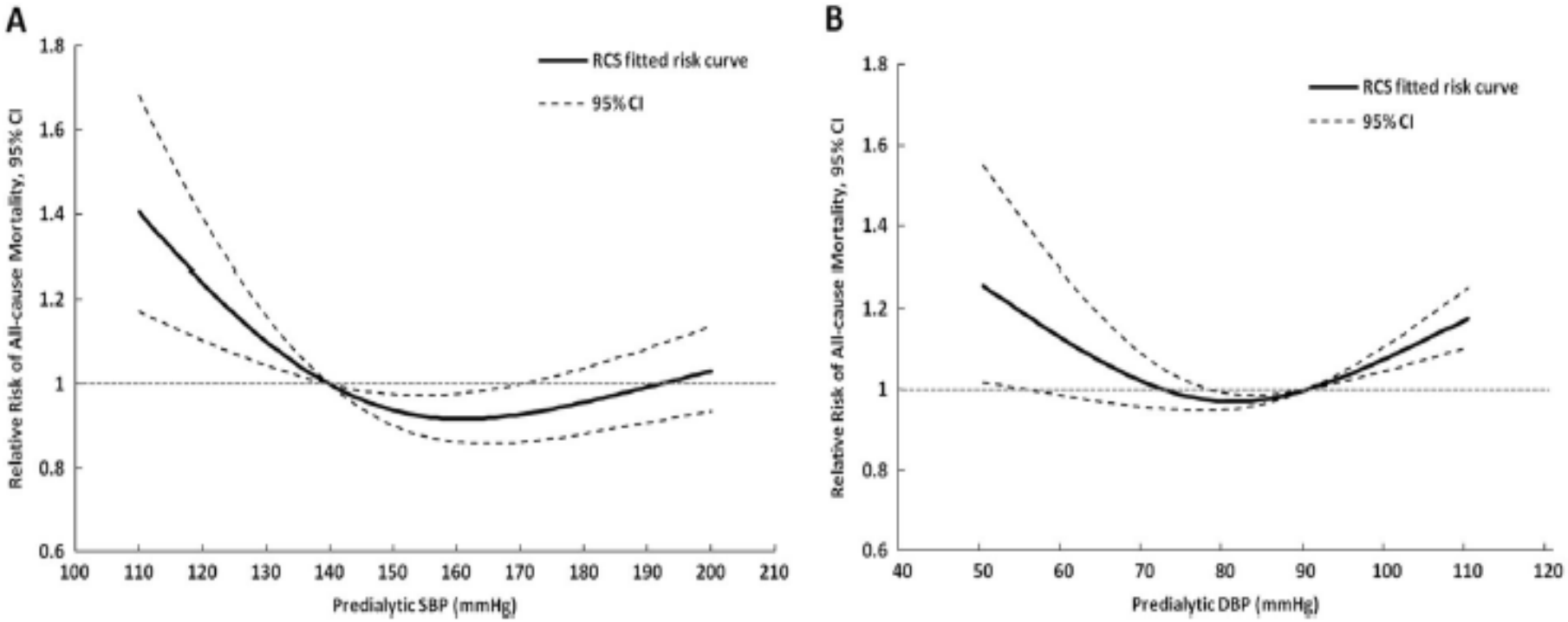
BP targets in ESRD-Guidelines

- 2005 K/DOQI guideline:

predialysis and postdialysis BP goals should be <140/90 mmHg and <130/80 mmHg, respectively. (Level C)

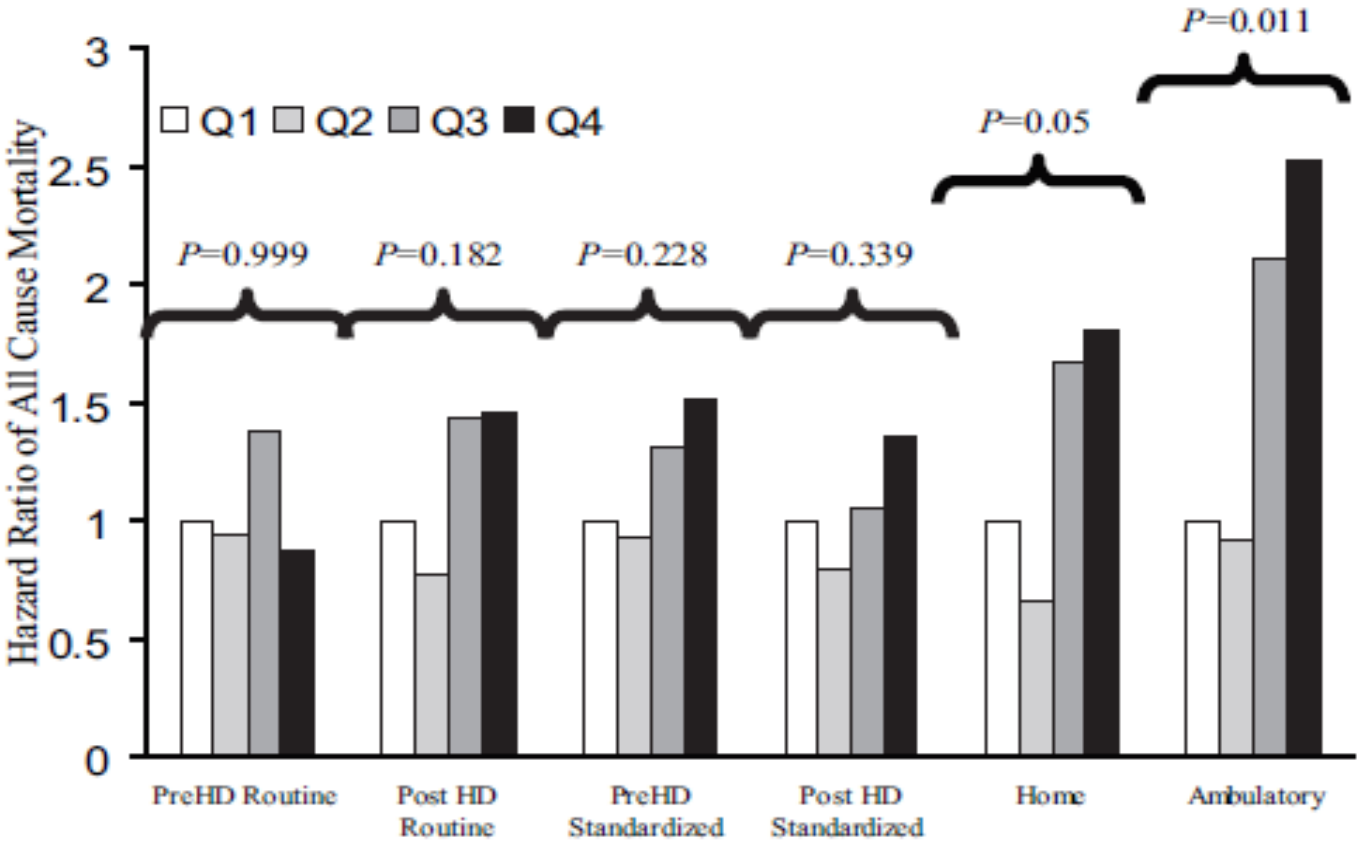
- 2012 KDIGO BP guideline: No recommendation.
- 2017 AHA/ACG guideline: No recommendation.
- 2018 ESH/ESC guideline: No recommendation.
- 2019 K/DOQI commentary on 2017 AHA/ACG guideline: No recommendation.
- 2021 KDIGO BP guideline: No recommendation.
- 2023 ESH guideline: No recommendation.

Association of hypertension with mortality in ESRD



Han Yu-Chen, et al. J Hum Hypertens 2019;33:41-49

Home Blood Pressures Are of Greater Prognostic Value than Hemodialysis Unit Recordings



Alborzi P, et al. Clin J Am Soc Nephrol 2007;2(6):1228-34.

The Relation of Clinic and Ambulatory BP with the Risk of Cardiovascular Events and All-Cause Mortality among Patients on Peritoneal Dialysis

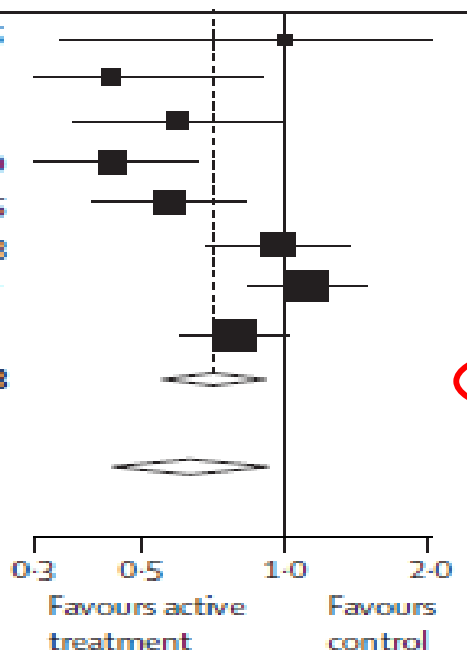
Table 2. Hazard ratio for the composite outcome of non-fatal MI, non-fatal stroke, or all-cause death according to the quartile of clinic and 24-h ambulatory SBP.

SBP		Unadjusted Analysis			Adjusted Analysis *		
Clinic	Range (mmHg)	HR	95% CI	*p* Value	HR	95% CI	*p* Value
Quartile 1	<119.2	1			1		
Quartile 2	119.2–132.0	0.201	0.057–0.711	<0.05	0.255	0.069–0.940	<0.05
Quartile 3	132.0–145.7	1.028	0.486–2.176	0.94	1.472	0.651–3.331	0.35
Quartile 4	>145.7	1.750	0.851–3.598	0.13	1.648	0.766–3.547	0.20
		Model fit (χ^2): 16.5 $p = 0.001$			Model fit (χ^2): 42.0 $p < 0.001$		
24-h Ambulatory							
Quartile 1	<114.0	1			1		
Quartile 2	114.0–126.0	0.667	0.280–1.586	0.36	1.098	0.434–2.777	0.84
Quartile 3	126.0–140.7	0.558	0.228–1.367	0.20	1.004	0.382–2.635	0.99
Quartile 4	>140.7	2.240	1.103–4.547	<0.05	2.449	1.156–5.190	<0.05
		Model fit (χ^2): 18.4 $p < 0.001$			Model fit (χ^2): 40.3 $p < 0.001$		

Georgianos PI, Vaios V, Liakopoulos V. J Clin Med 2021; 10(11):2232

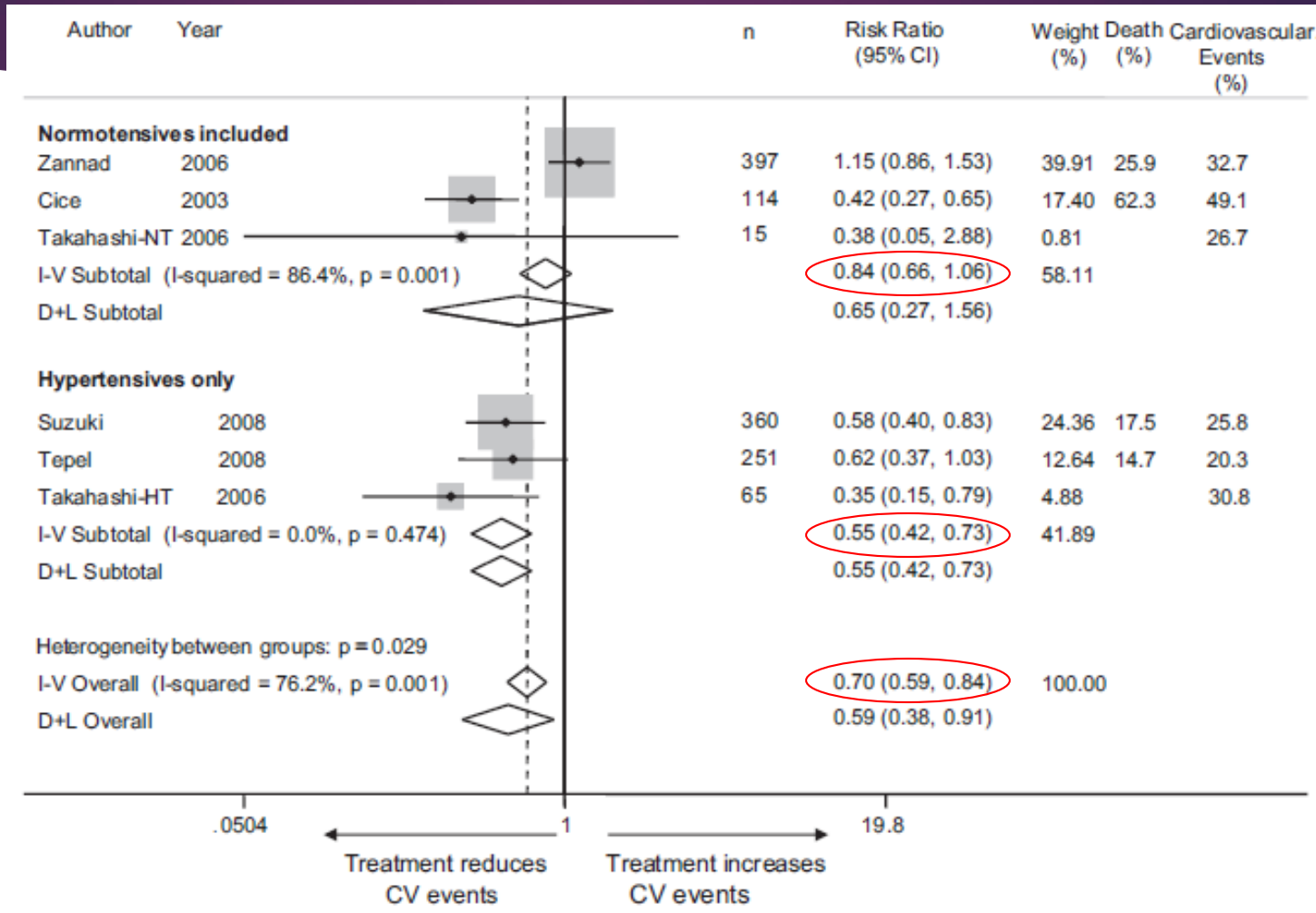
CV protection with antihypertensive agents in ESRD (1)

	Numbers of events/patients		SBP/DBP difference (mm Hg)	Risk ratio (95% CI)	Risk ratio (95% CI)
	Active treatment	Control			
Li et al (2003)[17]	5/30	5/30	+0·7/–3·5		1·00 (0·34–2·92)
Takahashi et al (2006)[19]	7/43	17/37	+3·0/0·0		0·43 (0·21–0·89)
Tepel et al (2008)[21]	19/123	32/128	–9·0/NA		0·60 (0·36–0·99)
Cice et al (2003)[10]	17/58	39/56	–10·5/–7·0		0·42 (0·27–0·65)
Suzuki et al (2008)[20]	34/183	59/183	–2·3/–0·5		0·58 (0·40–0·83)
Nakao et al (2007)[22]	NA/57	NA/51	–7·3/–6·3		0·97 (0·67–1·34)
Zannad et al (2006)[11]	67/196	60/201	–3·9/–1·7		1·12 (0·84–1·49)
Cice et al (2006)[18]	59/151	75/152	NA		0·79 (0·61–1·02)
Overall	**208/841**	**287/838**	**–4·5/–2·3**		**0·71 (0·55–0·92)**
Test for heterogeneity: I^2=67·5%, Q=21·5, p=0·003					
Excluding unpublished studies					**0·64 (0·43–0·94)**
Test for heterogeneity: I^2=73·7%, Q=19·0, p=0·002					



Lambers-Heerspink H, et al. Lancet 2009; 373: 1009–15.

CV protection with antihypertensive agents in ESRD (2)



Agarwal R. & Sinha AJ. Hypertension 2009;53(5):860-6.

BP targets in dialysis: BID trial

Blood Pressure in Dialysis (BID) Results of a Pilot Study

METHODS

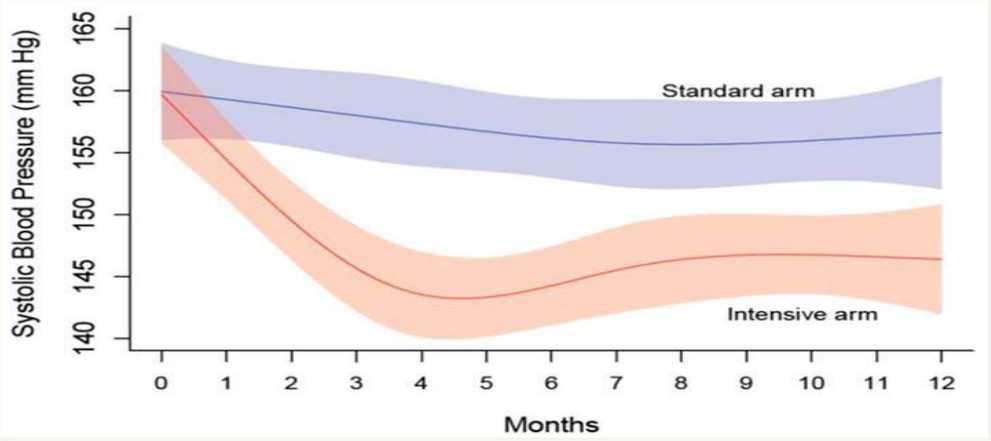
- A pilot RCT to assess feasibility and safety of conducting a full-scale trial of intensive control of hypertension in HD patients.
- Randomized 126 patients to a predialysis standardized SBP of 115-140 or 155-165 mm Hg for one year.

SAE Summary

Event	Hazard Ratio of Recurrent Events (95% CI)	P-value
MACE	0.89 (0.30 – 2.66)	0.84
Hospitalization	1.66 (1.18 – 2.34)	0.004
Vascular access thrombosis	2.80 (1.18 – 6.66)	0.020
Systolic blood pressure <90 mm Hg	1.30 (1.10 – 1.52)	0.002
Cramps	1.16 (1.04 – 1.30)	0.01
Nausea/vomiting	1.41 (1.02 – 1.94)	0.04

RESULTS

- Sustained separation in SBP.
- No significant reduction in MACE.
- Hospitalization, vascular access thrombosis, and intradialytic hypotension were increased in intensive arm.
- No difference in change in left ventricular mass across arms.



CONCLUSIONS

It is feasible to conduct a full-scale RCT. Given the study's small size and short duration the safety signal may not be a definitive result.

doi: 10.1681/ASN.

JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

Miskulin D, et al. J Am Soc Nephrol 2018; 29(2):571-578.

4) Treatment of HTN in ESRD
Non-pharmacological interventions

Volume management strategies

First-line management of hypertension in patients on dialysis should focus on:

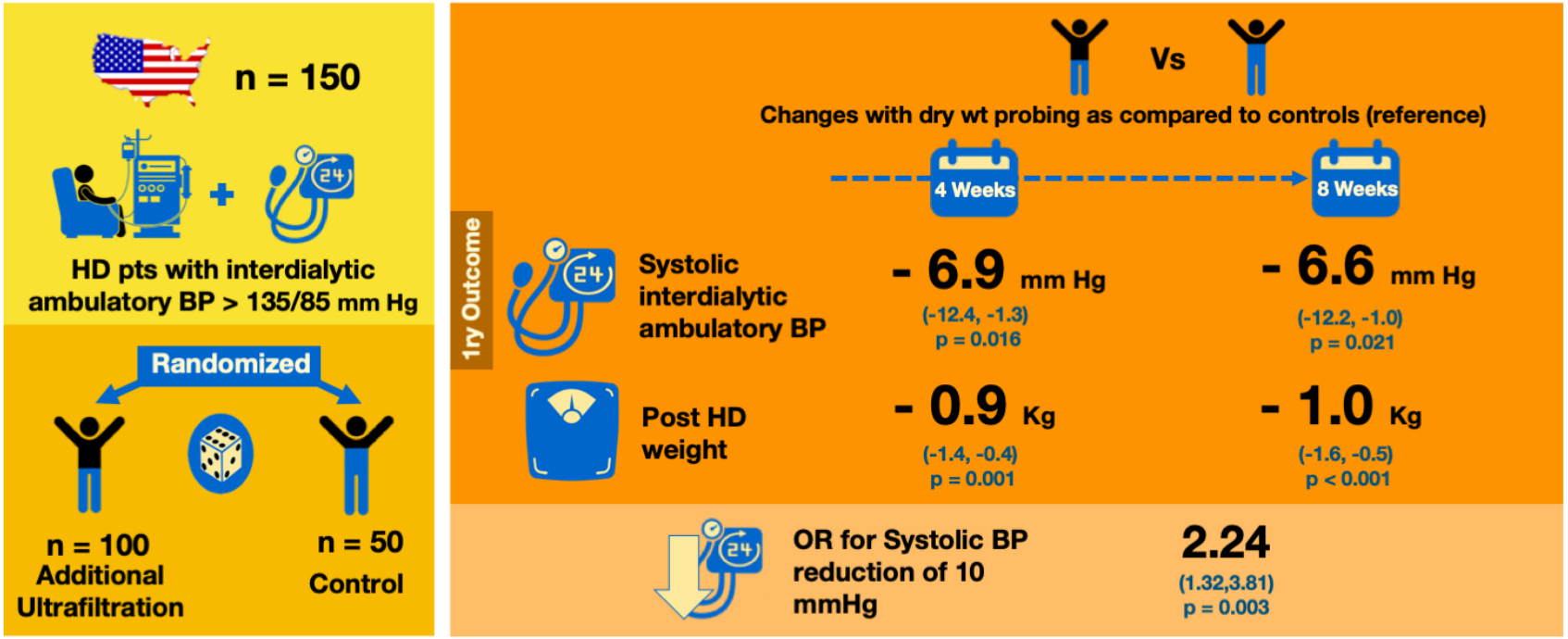
- ✓ *achieving dry weight*
- ✓ *lowering dietary Na^+*
- ✓ *individualizing dialysate Na^+ concentrations*
- ✓ *ensuring dialysis sessions are of adequate duration*

Georgianos PI & Agarwal R. Nat Rev Nephrol 2016;12(10):636-47.

Dry-Weight Reduction in Hypertensive Hemodialysis Patients (DRIP)

A Randomized, Controlled Trial

Does protocolized dry weight reduction improve BP in hypertensive hemodialysis patients? DRIP Trial



Conclusions Aggressive dry weight probing by protocol led to greater reduction in BP in hypertensive HD patients but also led to worse intradialytic signs and symptoms of hypotension.

Reference Agarwal R et al. Dry-weight reduction in hypertensive hemodialysis patients (DRIP): a randomized, controlled trial. Hypertension. 2009 Mar;53(3):500-7.

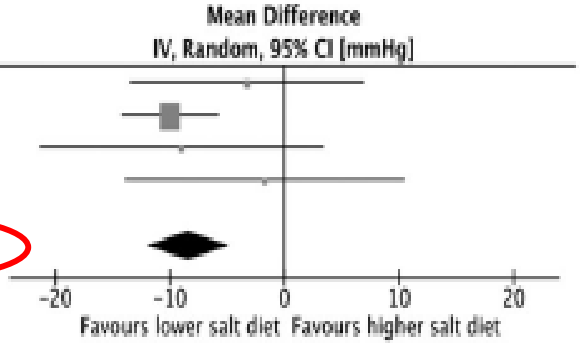
Agarwal R, et al. Hypertension 2009;53(3):500-7.

The effect of dietary salt on blood pressure in individuals receiving chronic dialysis: a systematic review and meta-analysis of randomised controlled trials

A

Study or Subgroup	Lower salt intake Mean [mmHg]	SD [mmHg]	Total	Higher salt intake Mean [mmHg]	SD [mmHg]	Total	Mean Difference IV, Random, 95% CI [mmHg]
Catto et al. (ref. 17)	136.9	13.9	15	140.2	14.7	15	-3.30 [-13.54, 6.94]
Doulton et al. (ref. 18)	119	4	11	129	6	11	-10.00 [-14.26, -5.74]
Fine et al. (ref. 19)	135	19	20	144	21	20	-9.00 [-21.41, 3.41]
Rodrigues Telini et al. (ref. 20)	147.5	18.3	21	149.2	20.4	18	-1.70 [-13.95, 10.55]
Total (95% CI)			67			64	**-8.38 [-11.97, -4.80]**

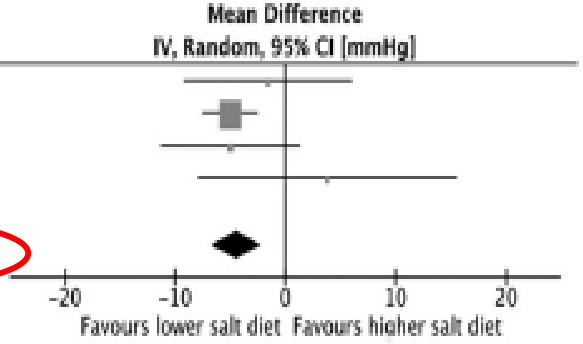
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.65$, df = 3 (P = 0.45); $I^2 = 0\%$
Test for overall effect: Z = 4.58 (P < 0.00001)



B

Study or Subgroup	Lower salt intake Mean [mmHg]	SD [mmHg]	Total	Higher salt intake Mean [mmHg]	SD [mmHg]	Total	Mean Difference IV, Random, 95% CI [mmHg]
Catto et al. (ref. 17)	84.2	10.5	15	85.8	10.8	15	-1.60 [-9.22, 6.02]
Doulton et al. (ref. 18)	66	3	11	71	3	11	-5.00 [-7.51, -2.49]
Fine et al. (ref. 19)	77	8	20	82	12	20	-5.00 [-11.32, 1.32]
Rodrigues Telini et al. (ref. 20)	87.4	11.9	21	83.6	22.9	18	3.80 [-7.94, 15.54]
Total (95% CI)			67			64	**-4.41 [-6.60, -2.22]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.65$, df = 3 (P = 0.45); $I^2 = 0\%$
Test for overall effect: Z = 3.95 (P < 0.0001)



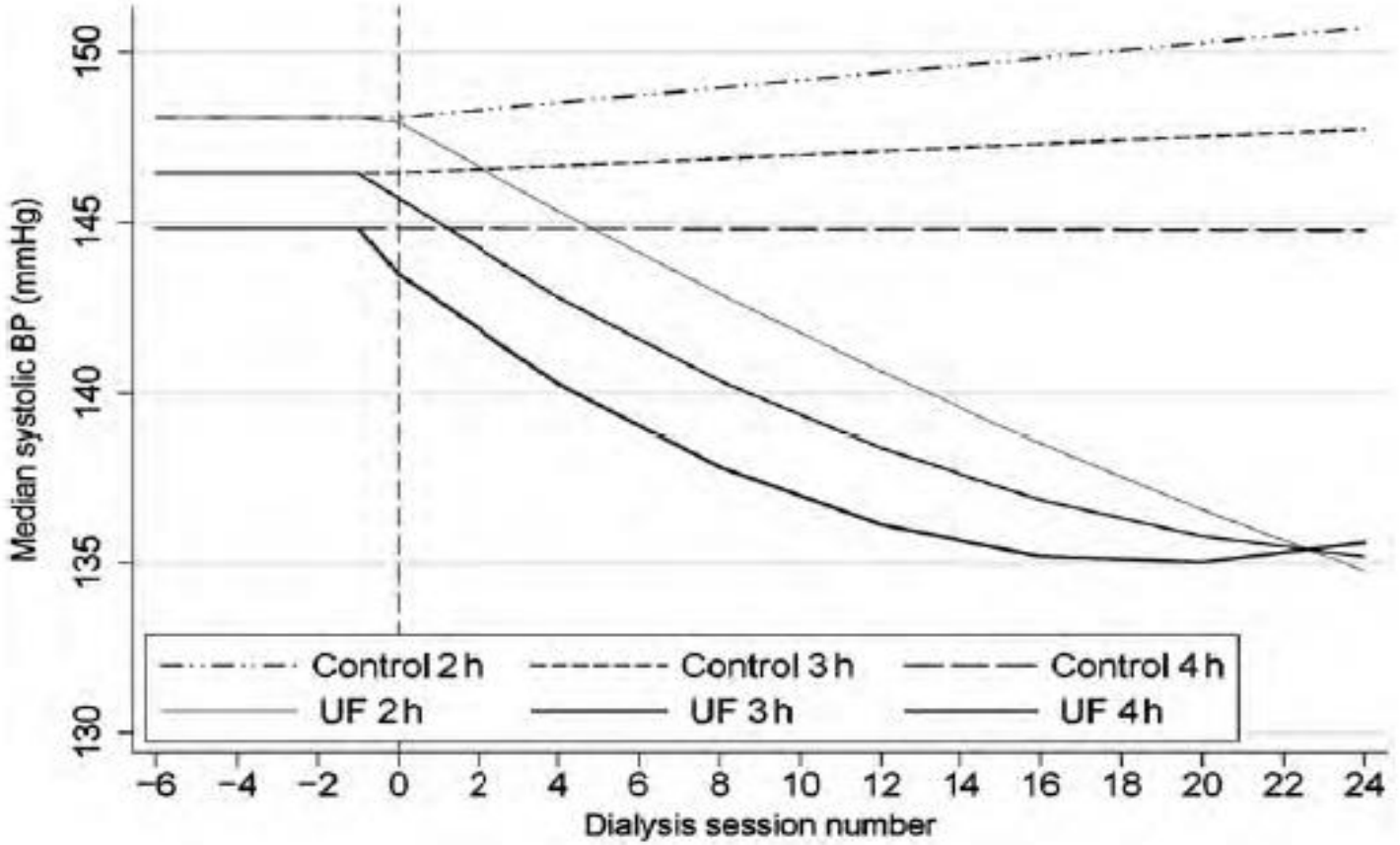
Cole N, et al. J Hum Hypertens 2019; 33:319-326.

Prescription of dialysate Na^+ concentration

Patients	*n*	Intervention	Follow-up	IDWG	BP	Intradialytic hypotension
Patients on standard HD	11	Standard HD (Na_d 138 mmol/l) versus sodium-profiling HD (Na_d 155–130 mmol/l or Na_d 150–130 mmol/l)	6 weeks	↓	↓	↑
Non-diabetic, non-hypoten-sion-prone HD patients	27	Individualized Na_d (set to match patients' average pre-HD plasma Na multiplied by the Donnan coefficient) versus standard HD with Na_d 138 mmol/l	3 weeks	↓	↓	↓
Patients on standard HD	52	Facility-wide lowering of Na_d from 141 mmol/l to 138 mmol/l	32 weeks	No change	↓	No change
Patients on standard HD	30	HD with Na_d 143 mmol/l versus HD with Na_d 137 mmol/l	6 weeks	↓	↓	↑
Patients on thrice-weekly nocturnal HD	15	Nocturnal HD with Na_d 140 mmol/l versus nocturnal HD with Na_d 136 mmol/l or 134 mmol/l followed by Na_d 140 mmol/l	12 weeks	↓	↓	No change
Patients on standard HD	41	Facility-wide lowering of Na_d from 140 mmol/l to 137 mmol/l	24 weeks	↓	No change	↑
Patients on standard HD	13	Individualized Na_d (set to progressively reach a sodium gradient between the dialysate and plasma level of –2 mmol/l)	12 weeks	↓	No change	No change
Patients on standard HD	16	HD with Na_d 138 mmol/l versus HD with Na_d 136 mmol/l	16 weeks	↓	↓	No change
Patients with intradialysis hypertension	16	HD with high Na_d (5 mmol/l above serum sodium level) versus HD with low Na_d (5 mmol/l below serum sodium level)	3 weeks	No change	↓	No change

Georgianos PI & Agarwal R. Nat Rev Nephrol 2016;12(10):636-47.

Shorter delivered dialysis times associate with a higher and more difficult to treat blood pressure



Tandon T, et al. Nephrol Dial Transplant 2013;28(6):1562-8.

5) Pharmacotherapy

Pharmacotherapy for HTN in ESRD: clinical trial evidence

Patients	*n*	Design	Intervention	Follow-up	Cardiovascular events	Mortality	Overall effect
Hypertension (not all patients) and LVH	397	Double-blind	Fosinopril (titrated up to 20 mg/day) versus placebo	48 months	No change	No change	Neutral
Without overt cardiovascular disease	80	Open-label	Candesartan (4–8 mg/day) versus nothing	36 months	↓	↓	Better
Hypertension	360	Open-label	Losartan (50–100 mg/day) or valsartan (80–160 mg/day) or candesartan (up to 12 mg/day) versus other therapy not including ACEIs or ARBs	36 months	↓	↓	Better
Hypertension	469	Open-label	Olmesartan (titrated up to 40 mg/day) versus other therapy not including ACEIs or ARBs	42 months	No change	No change	Neutral
Dilated cardiomyopathy	114	Double-blind	Carvedilol (titrated up to 25 mg twice daily) versus placebo	24 months	↓	↓	Better
Hypertension	251	Double-blind	Amlodipine (10 mg/day) versus placebo	19 months	↓	No change	Better
Oligoanuric	309	Open-label	Spironolactone (25 mg/day) versus nothing	36 months	↓	↓	Better
non-CHF patients on HD or PD	253	Open-label	Spironolactone (25 mg/day) versus placebo	24 months	↓	↓	Better

Georgianos PI & Agarwal R. Nat Rev Nephrol 2016;12(10):636-47.

Recommendations for the pharmacotherapy of HTN in predialysis CKD

	JNC 8	AHA/ACC	ESC/ESH	Hypertension Canada	KDIGO
Publication year	2014	2017	2018	2020	2021
Target: CKD (nondialysis), mm Hg	<140/90	<130/80	130–139/70–79	<120	<120
First-line agents in CKD (nondialysis)	ACE inhibitor or ARB for all CKD (grade B)	ACE inhibitor or ARB if greater than stage 3 CKD or stage 1–2 with ≥300 mg/d albuminuria	ACE inhibitor/ARB plus CCB or diuretic	ACE inhibitor/ARB if proteinuria, plus diuretics	ACE inhibitor or ARB if albuminuria with or without diabetes

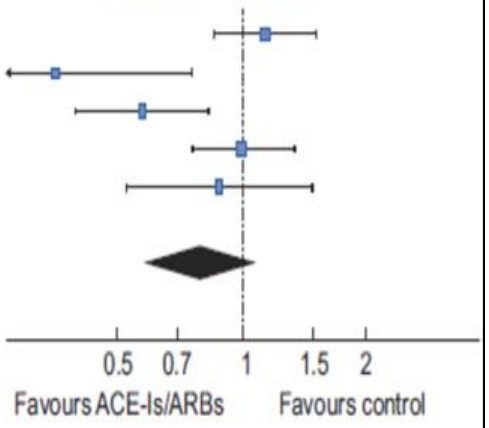
Bansal N et al. Hypertension. 2023 Jun;80(6):e112-e122.

Effect of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers on cardiovascular outcomes in dialysis patients: a systematic review and meta-analysis

Fatal/non-fatal CV events

Study or subgroup	ACE-Is/ARBs Events	Total	Control Events	Total	Weight	Risk ratio M-H, random, 95% CI	Year
Zannad 2006	67	196	60	201	24.4%	1.15 [0.86, 1.53]	2006
Takahashi 2006	7	43	17	37	11.9%	0.35 [0.17, 0.76]	2006
Suzuki 2008	34	183	59	183	21.9%	0.58 [0.40, 0.83]	2008
Iseki 2013	68	236	67	234	24.4%	1.01 [0.76, 1.34]	2013
Ruggenenti 2021	23	140	24	129	17.5%	0.88 [0.53, 1.48]	2021
Total (95% CI)		**798**		**784**	**100.0%**	**0.79 [0.57, 1.11]**	
Total events	199		227				

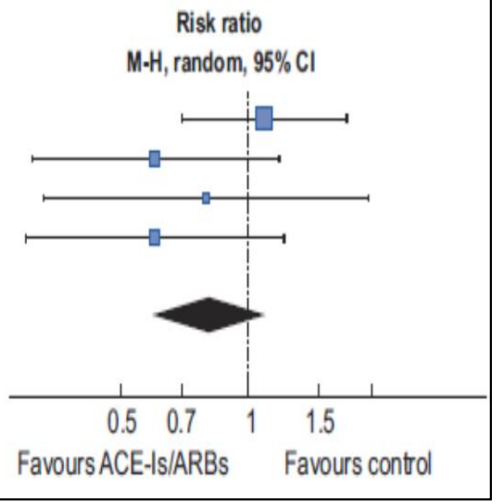
Heterogeneity: $\tau^2 = 0.10$; $\chi^2 = 14.66$, df = 4 (P = 0.005); $I^2 = 73\%$
Test for overall effect: Z = 1.33 (P = 0.18)



CV mortality

Study or subgroup	ACE-Is/ARBs Events	Total	Control Events	Total	Weight	Risk ratio M-H, random, 95% CI	Year
Zannad 2006	31	196	30	210	45.4%	1.11 [0.70, 1.76]	2006
Suzuki 2008	12	183	20	183	21.9%	0.60 [0.30, 1.19]	2008
Iseki 2013	8	235	10	234	12.7%	0.80 [0.32, 1.98]	2013
Ruggenenti 2021	11	140	17	129	20.0%	0.60 [0.29, 1.22]	2021
Total (95% CI)		**754**		**756**	**100.0%**	**0.82 [0.59, 1.14]**	
Total events	62		77				

Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 3.18$, df = 3 (P = 0.37); $I^2 = 6\%$
Test for overall effect: Z = 1.18 (P = 0.24)



Georgianos PI, et al. Nephrol Dial Transplant 2023; 38: 203-211

RCTs with ACEIs or ARBs in PD

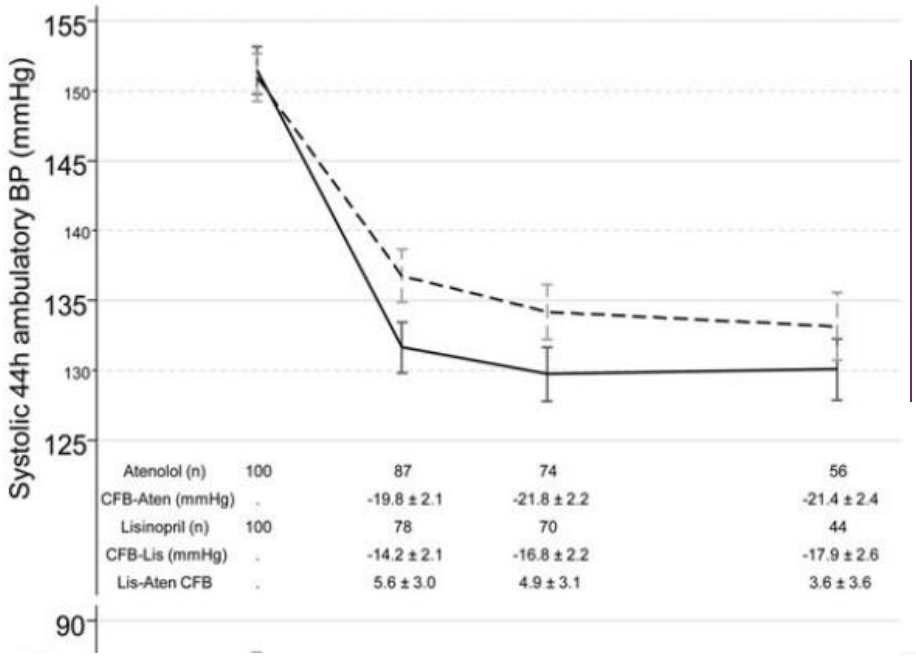
Author	Year	*N*	Characteristics	Design	Intervention	Follow-Up, mo	Primary Outcome	Overall Effect	Details
Li *et al.* (53)	2003	60	Patients on PD with residual kidney function	Open-label	Ramipril (5 mg/d) versus no treatment	12	Rate of decline in residual GFR or complete anuria	Better	Ramipril was superior to no treatment in reducing the incidence of complete anuria (HR, 58%; 95% CI, 36% to 94%)
Suzuki *et al.* (55)	2003	24	Patients on PD with LV hypertrophy	Double-blind	Valsartan (160 mg/d) versus placebo	12	Change in LV mass index	Better	Compared with placebo, valsartan therapy caused a greater regression of LV mass index (145±5 versus 121±4 g/m^2; $P<0.05$)
Suzuki *et al.* (56)	2004	34	Patients on PD with hypertension and residual kidney function	Open-label	Valsartan (40–80 mg/d) versus other therapy not including ACEIs/ARBs	24	Rate of decline in residual GFR	Better	Valsartan retarded the loss of residual kidney function during follow-up (3.2±0.3 versus 4.3±0.7 ml/min per 1.73 m^2), despite the absence of significant between-group difference in mean follow-up BP levels
Shigenaga *et al.* (54)	2009	45	Patients on PD with hypertension	Open-label	Candesartan (16 mg/d) or valsartan (160 mg/d) or other therapy not including ACEIs/ARBs	6	Change in LV mass index and baPWV	Better	Despite the absence of significant between-group difference in change of 24-h ambulatory BP, ARBs were superior to control therapy in causing regression of LV mass index and baPWV

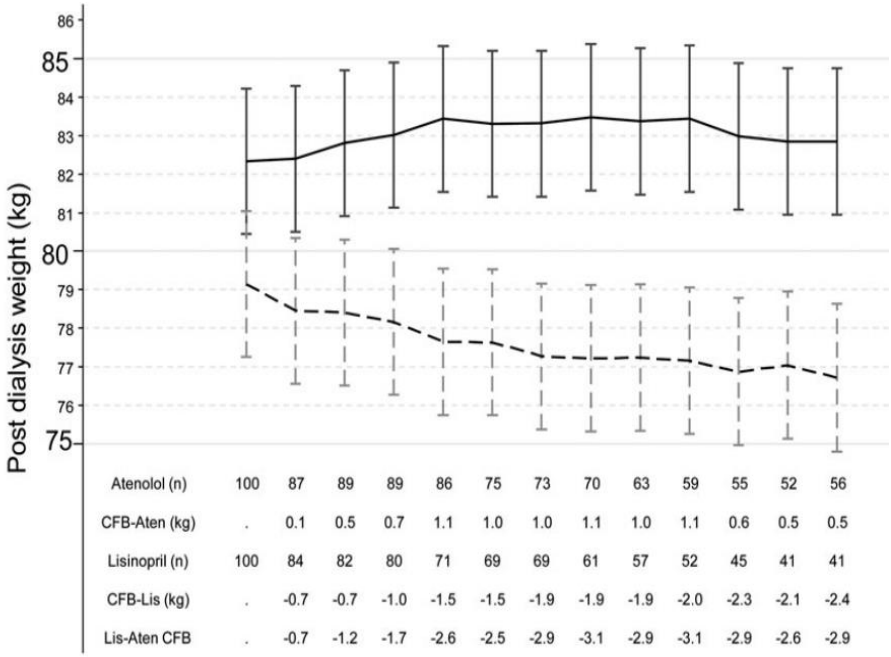
Vaios V, et al. Clin J Am Soc Nephrol 2019; 14:297-305

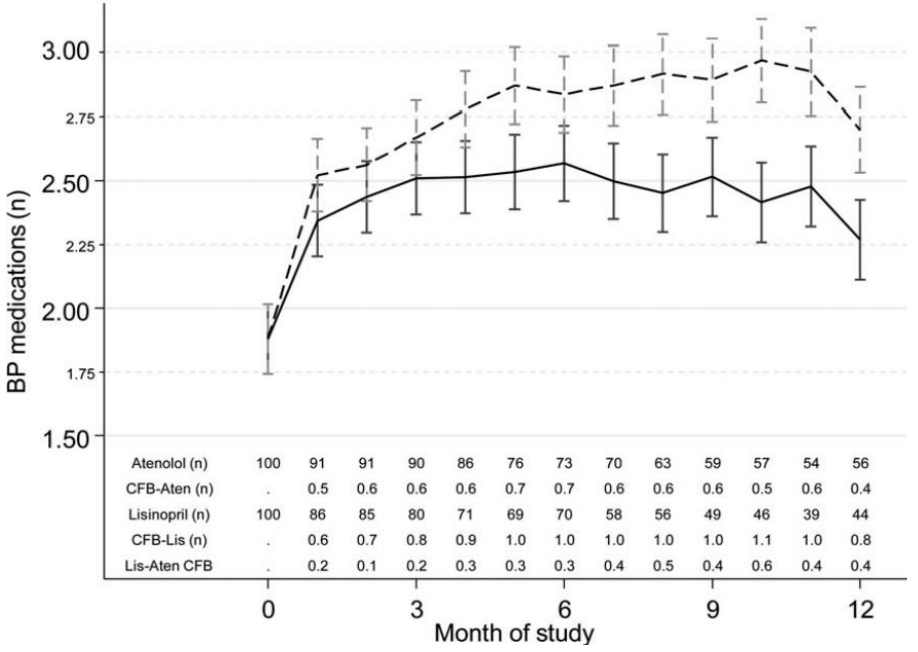
Atenolol vs Lisinopril in HD: the HDPAL trial

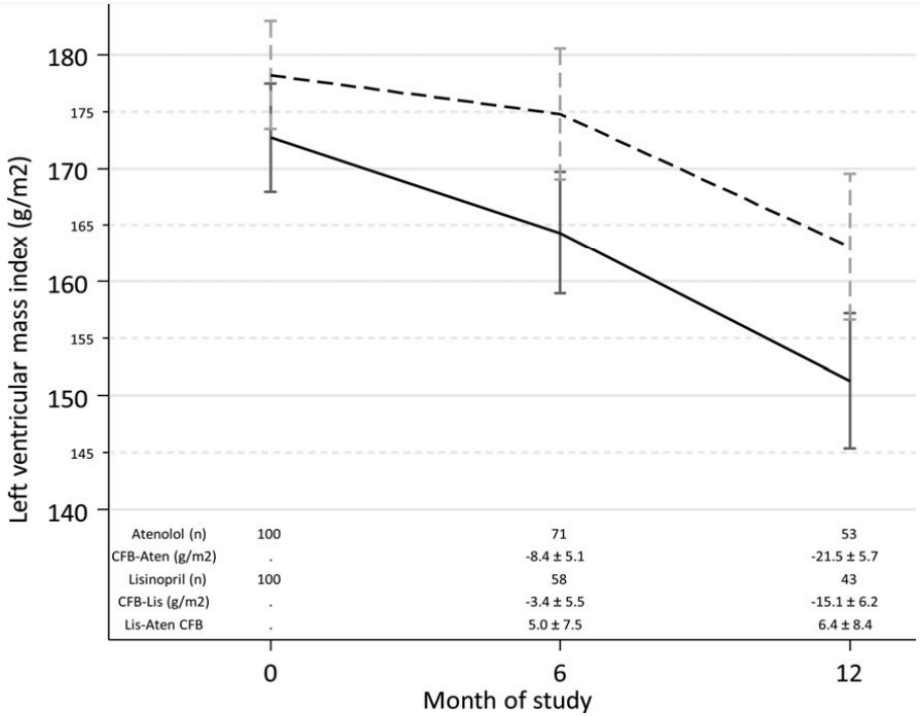
- ✓ **200 HD patients** → 100: Atenolol TIW; 100: Lisinopril TIW
- ✓ **12-month period**
- ✓ **BP monitoring: HBPM (monthly) and 44h interdialytic ABPM (every 3 months)**
- ✓ **Primary outcome: between group differences in change from baseline (CFB) to 12 months in LVMI**

Agarwal R, et al. Nephrol Dial Transplant 2014; 29: 672-681.


Systolic 44h ambulatory BP (mmHg)
155
150
145
140
135
130
125
90
Atenolol (n) 100 87 74 56
CFB-Aten (mmHg) . -19.8 ± 2.1 -21.8 ± 2.2 -21.4 ± 2.4
Lisinopril (n) 100 78 70 44
CFB-Lis (mmHg) . -14.2 ± 2.1 -16.8 ± 2.2 -17.9 ± 2.6
Lis-Aten CFB . 5.6 ± 3.0 4.9 ± 3.1 3.6 ± 3.6


Post dialysis weight (kg)
86
85
84
83
82
81
80
79
78
77
76
75
Atenolol (n) 100 87 89 89 86 75 73 70 63 59 55 52 56
CFB-Aten (kg) . 0.1 0.5 0.7 1.1 1.0 1.0 1.1 1.0 1.1 0.6 0.5 0.5
Lisinopril (n) 100 84 82 80 71 69 69 61 57 52 45 41 41
CFB-Lis (kg) . -0.7 -0.7 -1.0 -1.5 -1.5 -1.9 -1.9 -1.9 -2.0 -2.3 -2.1 -2.4
Lis-Aten CFB . -0.7 -1.2 -1.7 -2.6 -2.5 -2.9 -3.1 -2.9 -3.1 -2.9 -2.6 -2.9


BP medications (n)
3.00
2.75
2.50
2.25
2.00
1.75
1.50
Atenolol (n) 100 91 91 90 86 76 73 70 63 59 57 54 56
CFB-Aten (n) . 0.5 0.6 0.6 0.6 0.7 0.7 0.6 0.6 0.6 0.5 0.6 0.4
Lisinopril (n) 100 86 85 80 71 69 70 58 56 49 46 39 44
CFB-Lis (n) . 0.6 0.7 0.8 0.9 1.0 1.0 1.0 1.0 1.0 1.1 1.0 0.8
Lis-Aten CFB . 0.2 0.1 0.2 0.3 0.3 0.3 0.4 0.5 0.4 0.6 0.4 0.4
0
3
6
9
12
Month of study


Left ventricular mass index (g/m2)
180
175
170
165
160
155
150
145
140
Atenolol (n) 100 71 53
CFB-Aten (g/m2) . -8.4 ± 5.1 -21.5 ± 5.7
Lisinopril (n) 100 58 43
CFB-Lis (g/m2) . -3.4 ± 5.5 -15.1 ± 6.2
Lis-Aten CFB . 5.0 ± 7.5 6.4 ± 8.4
0
6
12
Month of study

Hypertension in hemodialysis patients treated with atenolol or lisinopril: a randomized controlled trial

Event type	Atenolol			Lisinopril				
	Subjects (*n*)	Events (*n*)	Incidence rate(events/ 100patient-years)	Subjects (*n*)	Events (*n*)	Incidence rate(events/ 100patient-years)	IRR Lisinopril/atenolol (95% CI)	P
Overall serious adverse events	58	140	172.4	70	188	253.6	1.47 (1.18–1.84)	<0.001
All-cause hospitalization rate	37	73	89.9	59	107	144.3	1.61 (1.18–2.19)	0.002
Infections	24	30	36.9	20	29	39.1	1.07 (0.62–1.85)	0.78
Access-related	17	24	29.6	19	30	40.5	1.28 (0.73–2.30)	0.36
Central nervous system	3	3	3.7	3	5	6.7	1.81 (0.35–11.63)	0.44
Cancer-related complications	2	4	4.9	2	3	4	0.82 (0.12–4.85)	0.81
Cardiovascular events	16	20	24.6	28	43	58	2.36 (1.36–4.23)	0.001
Combined MI, Stroke, CHF,	10	11	13.5	17	23	31	2.29 (1.07–5.21)	0.02
CV-related Death								
Angina	0	0	0	2	2	2.7	NA	
Arrhythmia	2	2	2.5	3	5	6.7	2.75 (0.45–28.88)	0.24
Cardiac arrest	0	0	0	2	2	2.7	NA	
Congestive heart failure	5	5	6.2	10	15	20.2	3.13 (1.08–10.99)	0.02
Myocardial infarction	2	2	2.5	3	3	4	1.61 (0.18–19.26)	0.63
Peripheral vascular disease	1	1	1.2	5	6	8.1	6.35 (0.77–291.93)	0.06
Revascularization	3	4	4.9	4	4	5.4	1.08 (0.20–5.82)	0.91
Stroke	2	2	2.5	2	2	2.7	1.10 (0.08–15.11)	0.93
Valve replacement surgery	1	1	1.2	1	1	1.3	1.10 (0.01–86.00)	0.95
Cardiovascular death	2	2	2.5	3	3	4	1.61 (0.18–19.23)	0.63

Agarwal R, et al. Nephrol Dial Transplant 2014; 29: 672-681.

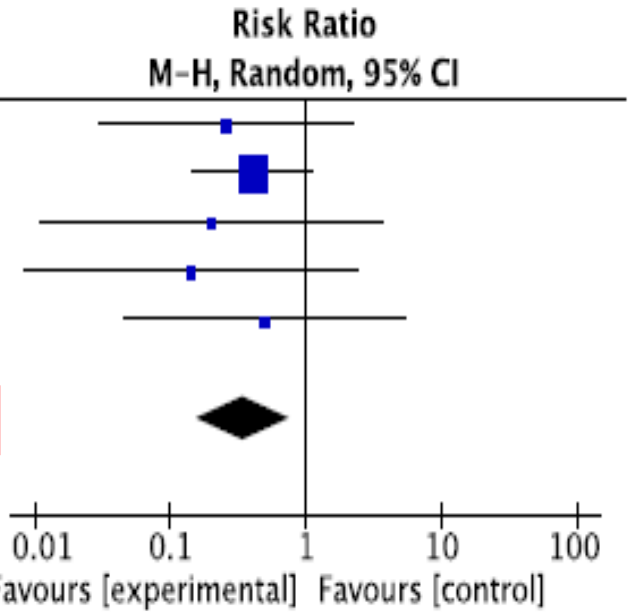
The Safety and Efficacy of Mineralocorticoid Receptor Antagonists in Patients Who Require Dialysis: A Systematic Review and Meta-analysis

Effect of MRAs on CV mortality

Study or Subgroup	MRA Events	MRA Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Ito 2013	1	78	4	80	13.3%	0.26 [0.03, 2.24]
Matsumoto 2014	5	157	12	152	60.3%	0.40 [0.15, 1.12]
Taheri 2009	0	8	2	8	7.5%	0.20 [0.01, 3.61]
Taheri 2012	0	9	3	9	7.8%	0.14 [0.01, 2.42]
Walsh 2015	1	77	2	77	11.1%	0.50 [0.05, 5.40]
Total (95% CI)		**329**		**326**	**100.0%**	**0.34 [0.15, 0.75]**
Total events	7		23			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.77$, df = 4 (P = 0.94); $I^2 = 0\%$

Test for overall effect: Z = 2.67 (P = 0.008)



Quach K, et al. Am J Kidney Dis 2016; 68: 591-98.

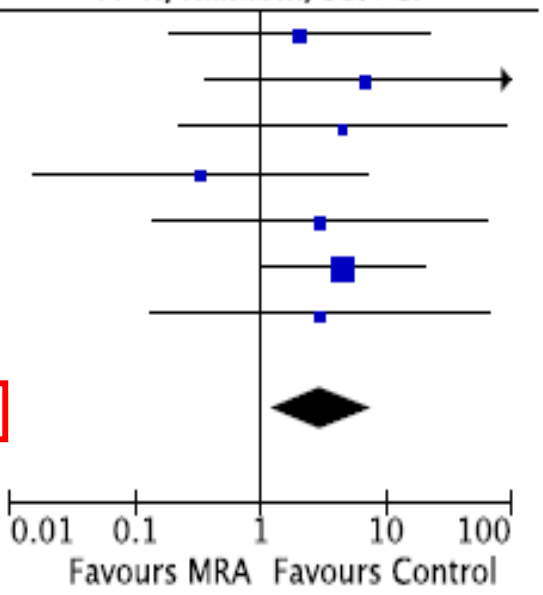
The Safety and Efficacy of Mineralocorticoid Receptor Antagonists in Patients Who Require Dialysis: A Systematic Review and Meta-analysis

Effect of MRAs on hyperkalemia

	MRA		Placebo			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Ito 2013	2	78	1	80	15.2%	2.05 [0.19, 22.17]	
Matsumoto 2014	3	157	0	152	9.9%	6.78 [0.35, 130.14]	
Ni 2014	2	40	0	36	9.5%	4.51 [0.22, 90.96]	
Taheri 2009	0	8	1	8	9.2%	0.33 [0.02, 7.14]	
Taheri 2012	1	9	0	9	9.1%	3.00 [0.14, 65.16]	
Walsh 2015	9	77	2	77	38.3%	4.50 [1.00, 20.15]	
Yongsiri 2015	1	12	0	12	8.9%	3.00 [0.13, 67.06]	
Total (95% CI)		**381**		**374**	**100.0%**	**3.05 [1.21, 7.70]**	
Total events	18		4				

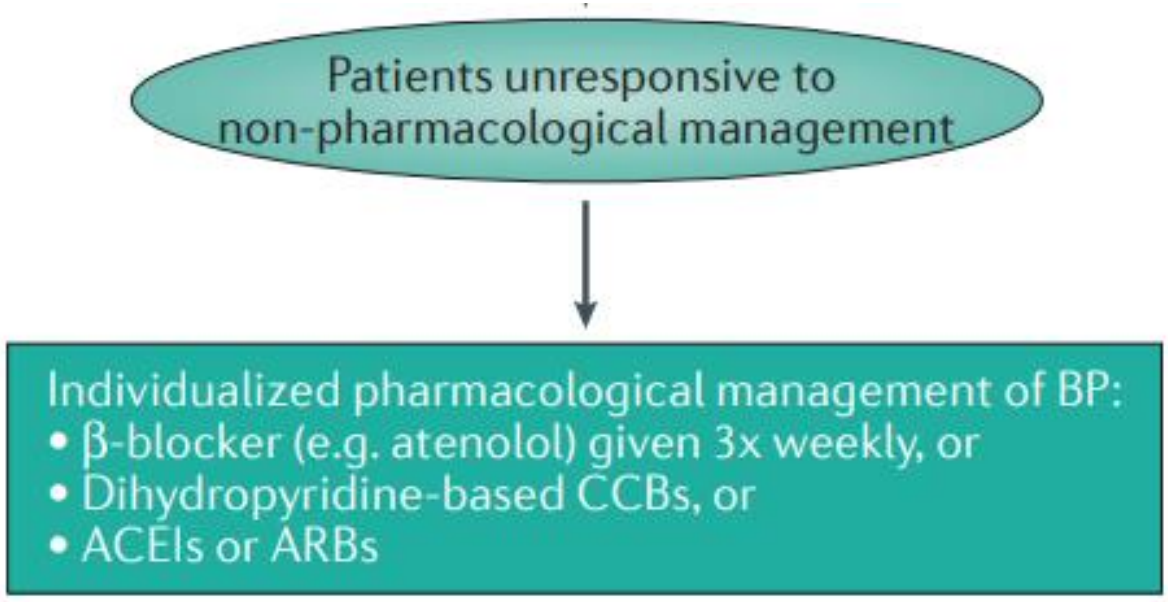
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.72$, df = 6 (P = 0.84); $I^2 = 0\%$

Test for overall effect: Z = 2.35 (P = 0.02)



Quach K, et al. Am J Kidney Dis 2016; 68: 591-98.

Pharmacotherapy for HTN in ESRD



Georgianos PI & Agarwal R. Nat Rev Nephrol 2016;12(10):636-47.


ΑΧΕΠΑ
ΠΑΝΕΠΙΣΤΗΜΙΑΚΟ ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΘΕΣΣΑΛΟΝΙΚΗΣ ΑΧΕΠΑ