Treatment of Hypertension in Patients on Hemodialysis

Hermann Haller
Department of Nephrology
Hannover Medical School

Blood pressure treatment - “conventional“ wisdom in ESRD patients

Salt ???
Changes over time ???

Blood pressure regulation

volume-dependent
Salt/water

Heart failure

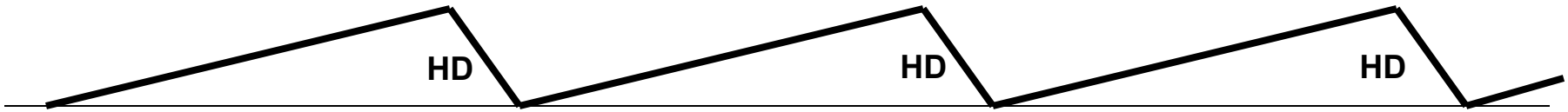
vasoconstriction

RAS, sympathetic activity, lack of NO, medullipin etc.

Arterial compliance

calcification

What is the “real” RR ???



Acute changes ???

Definition of Hypertension

K/DOQI 2005 guidelines on cardiovascular disease in dialysis patients

Predialysis and postdialysis blood pressure goals should be <140/90mmHg and <130/80mmHg respectively (C)

K/DOQI 2006 update of hemodialysis adequacy guidelines

Focus on volume control, dietary sodium restriction and avoidance of high dialysate sodium

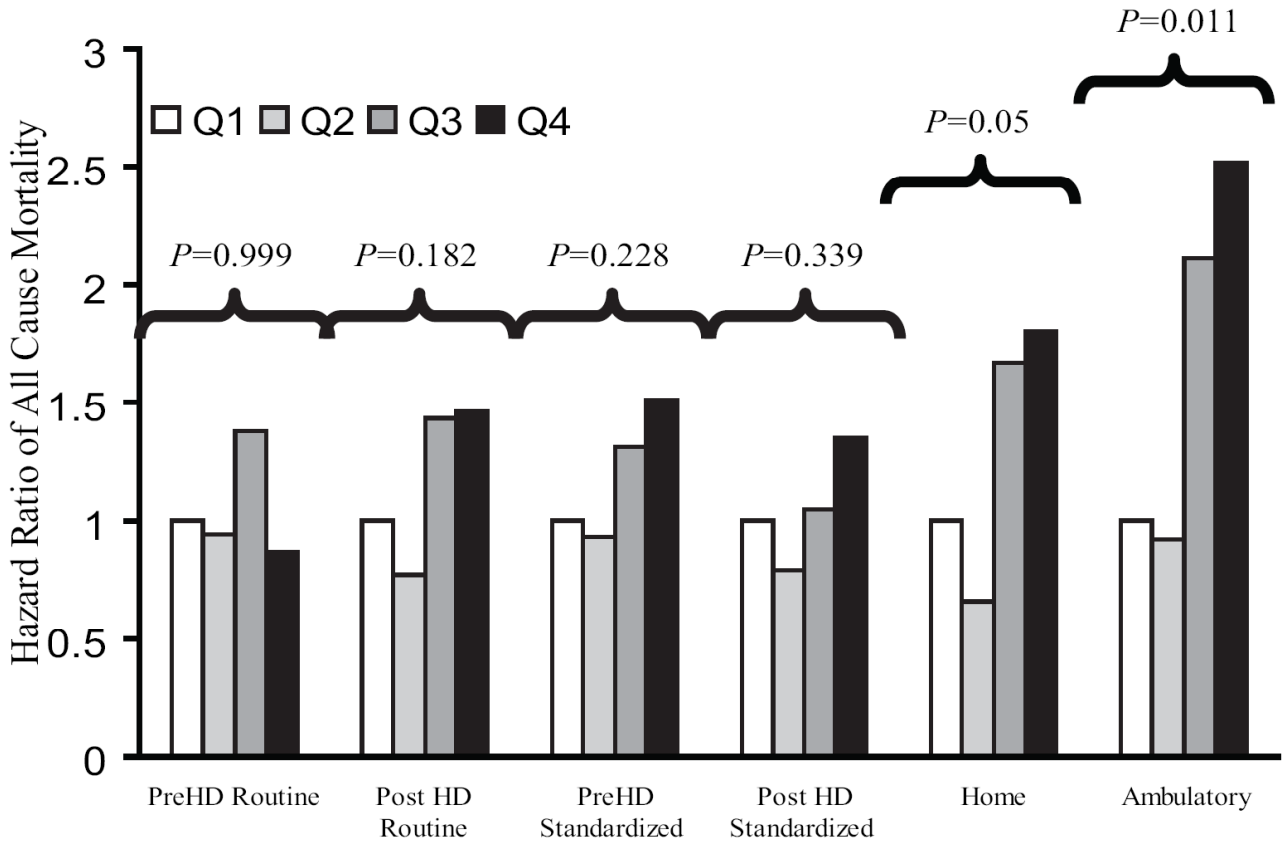
DO NOT recommend specific blood pressure targets in hemodialysis patients

K/DOQI 2007 clinical practice guidelines for diabetes and CKD

Target blood pressure in diabetes and CKD stages 1-4 should be <130/80mmHg (B)

Targets for patients on dialysis are not recommended.

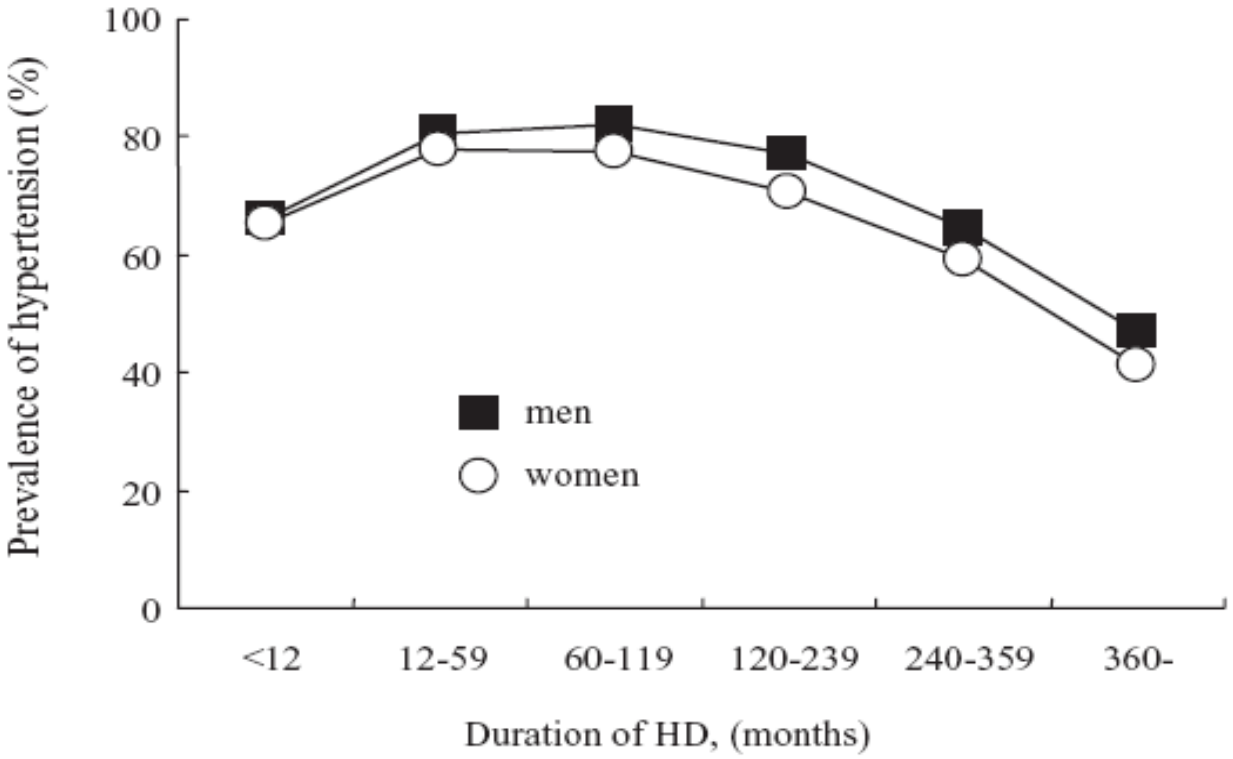
Home blood pressure monitoring is of greater prognostic value than hemodialysis units recordings



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

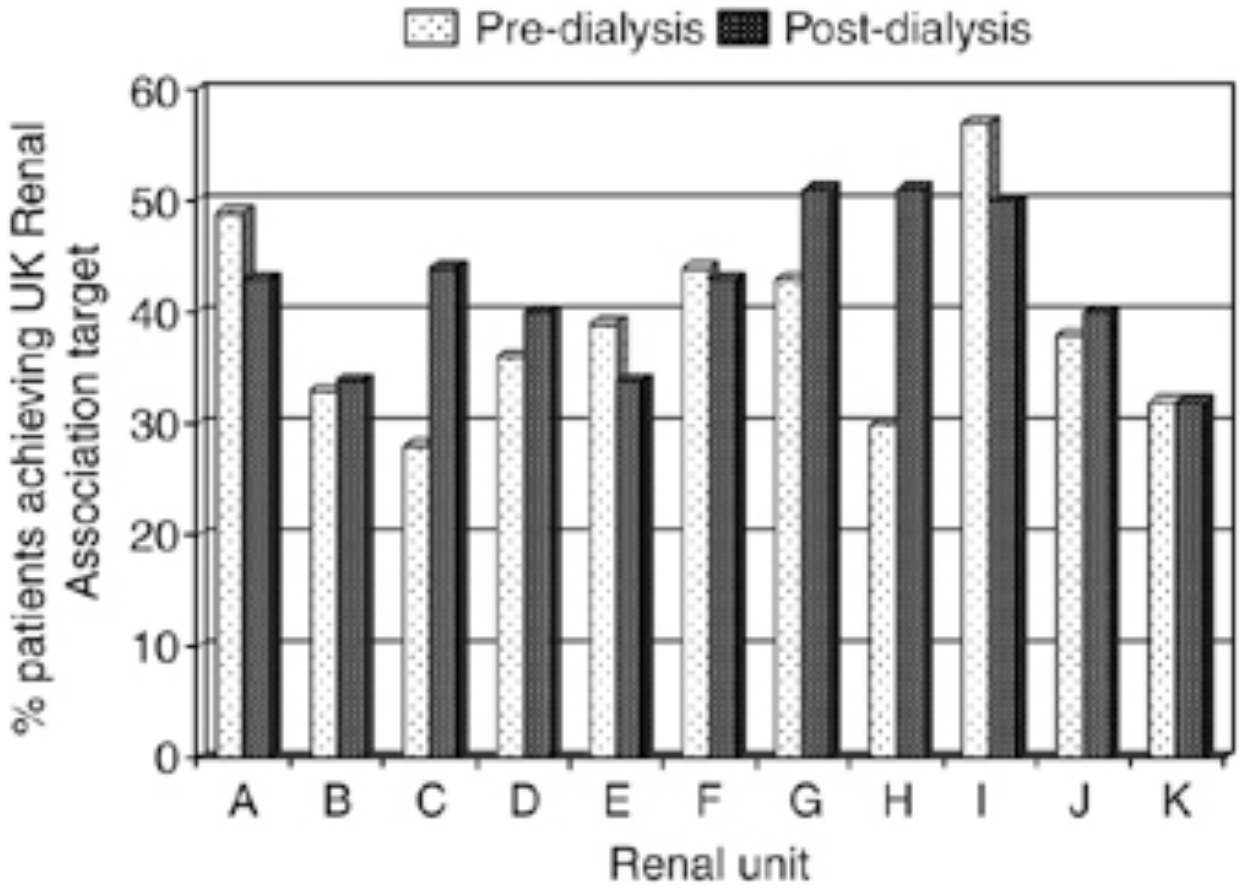
Prevalence of hypertension in chronic HD pts

(N=65393, mean age 61 yr, mean duration on HD 8 yr)



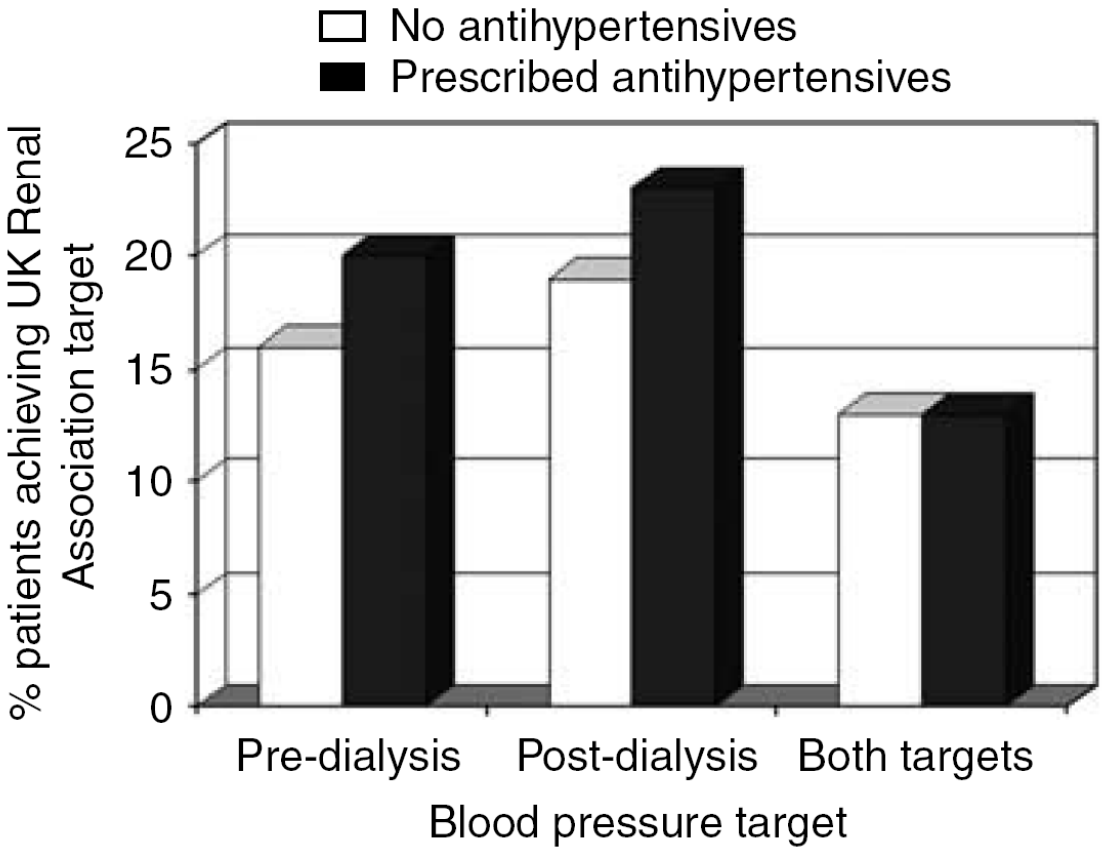
Iseki et al. Ther Apher Dial 2007;11:183-188

Patients achieving pre- and post-dialysis UK RA blood pressure targets (<140/90 or <130/80 mm Hg)



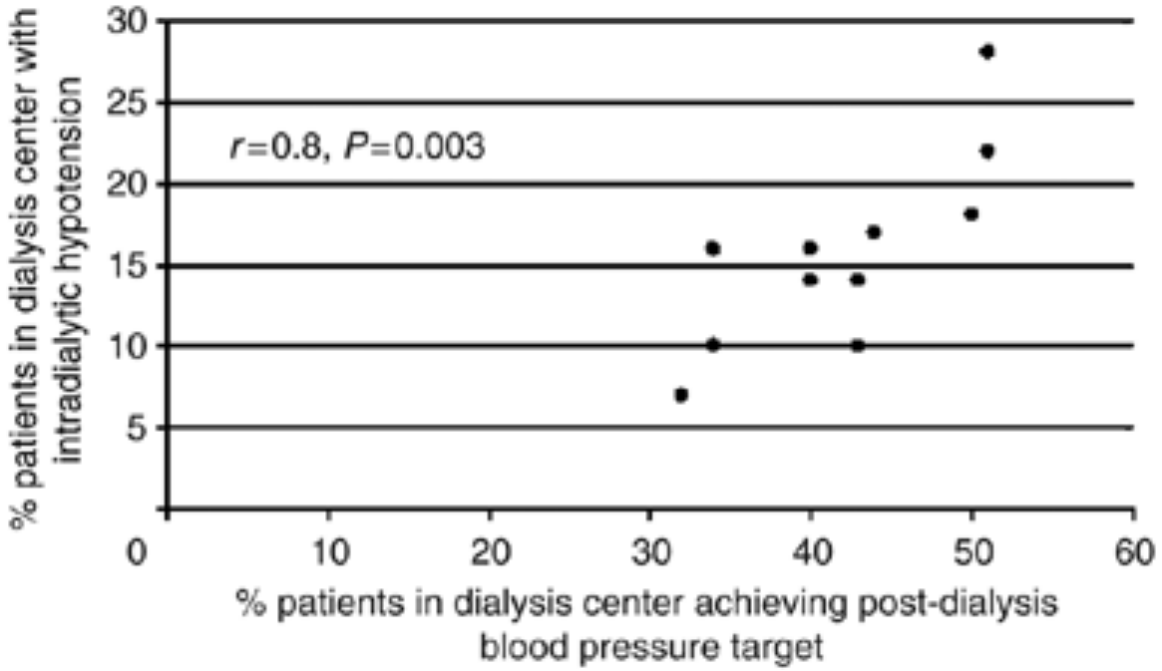
Davenport et al. Kidney International 2008; 73: 759-754

Blood pressure control rates in a cohort of hemodialysis patients (N=2360)



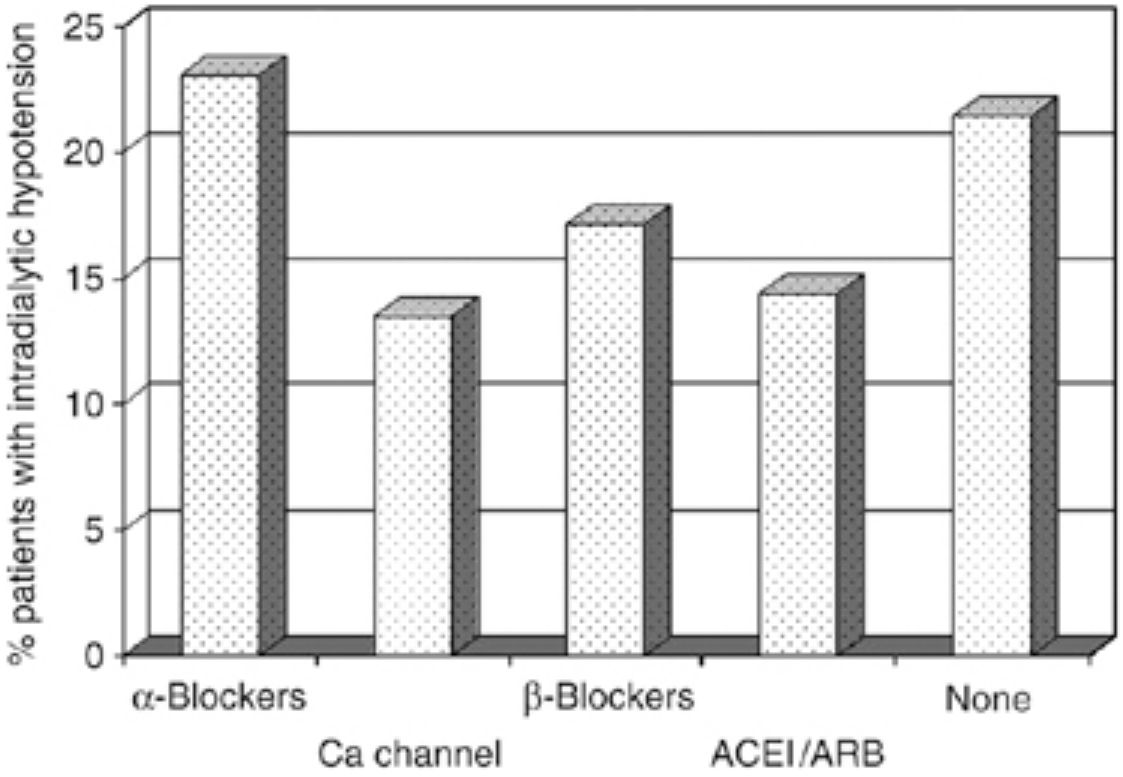
Davenport et al. Kidney International 2008; 73: 759-754

Patients achieving post-dialysis UK RA blood pressure targets and intradialytic hypotension



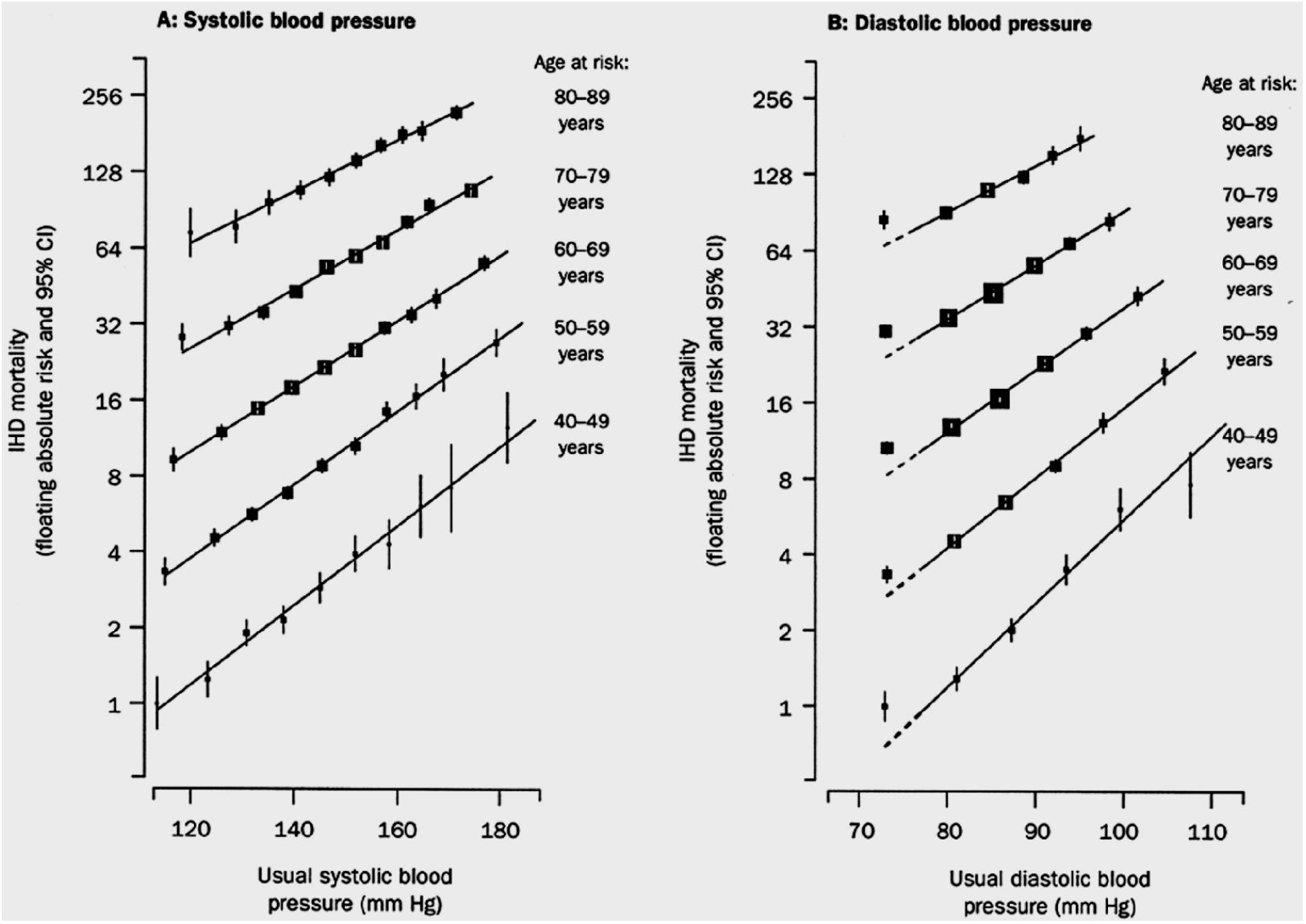
Davenport et al. Kidney International 2008; 73: 759-754

The effects of different drug classes on intradialytic hypotension



Davenport et al. Kidney International 2008; 73: 759-754

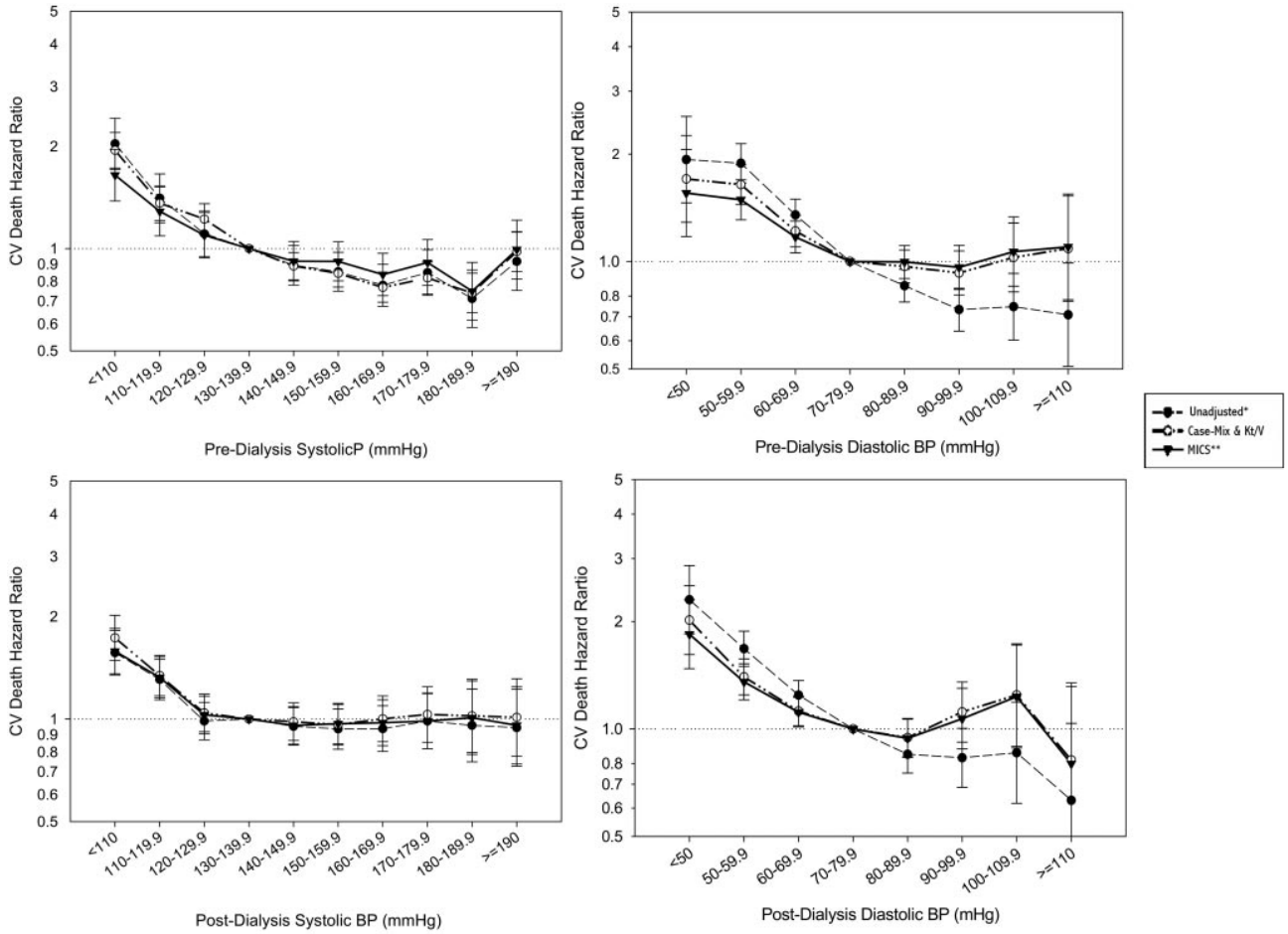
Blood pressure and coronary artery disease



Prospective Studies Collaboration, Lancet 2002;360:1903

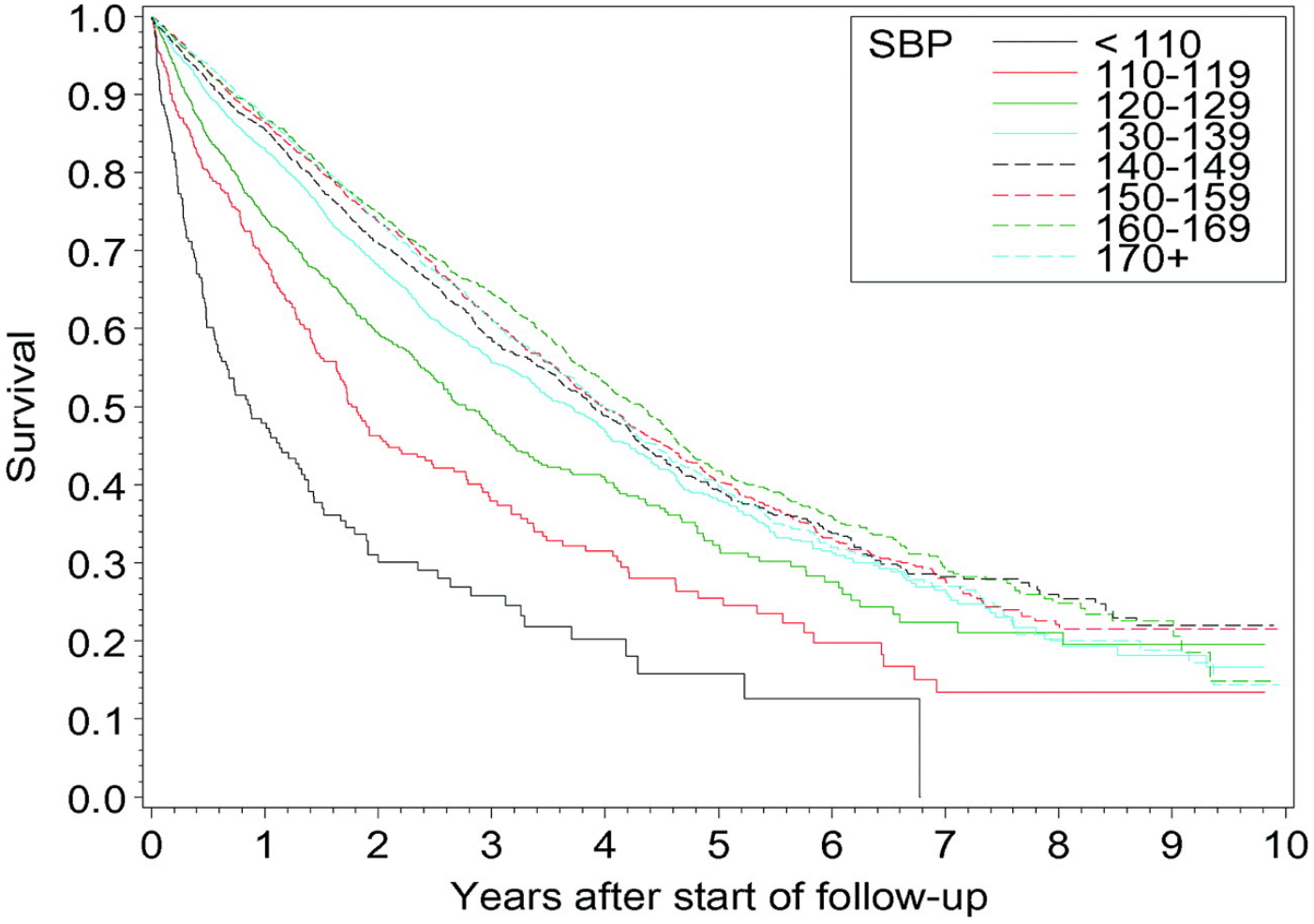
Association between BP and 15-month CV death in 40 933 MHD patients

(95% confidence interval bars are depicted)



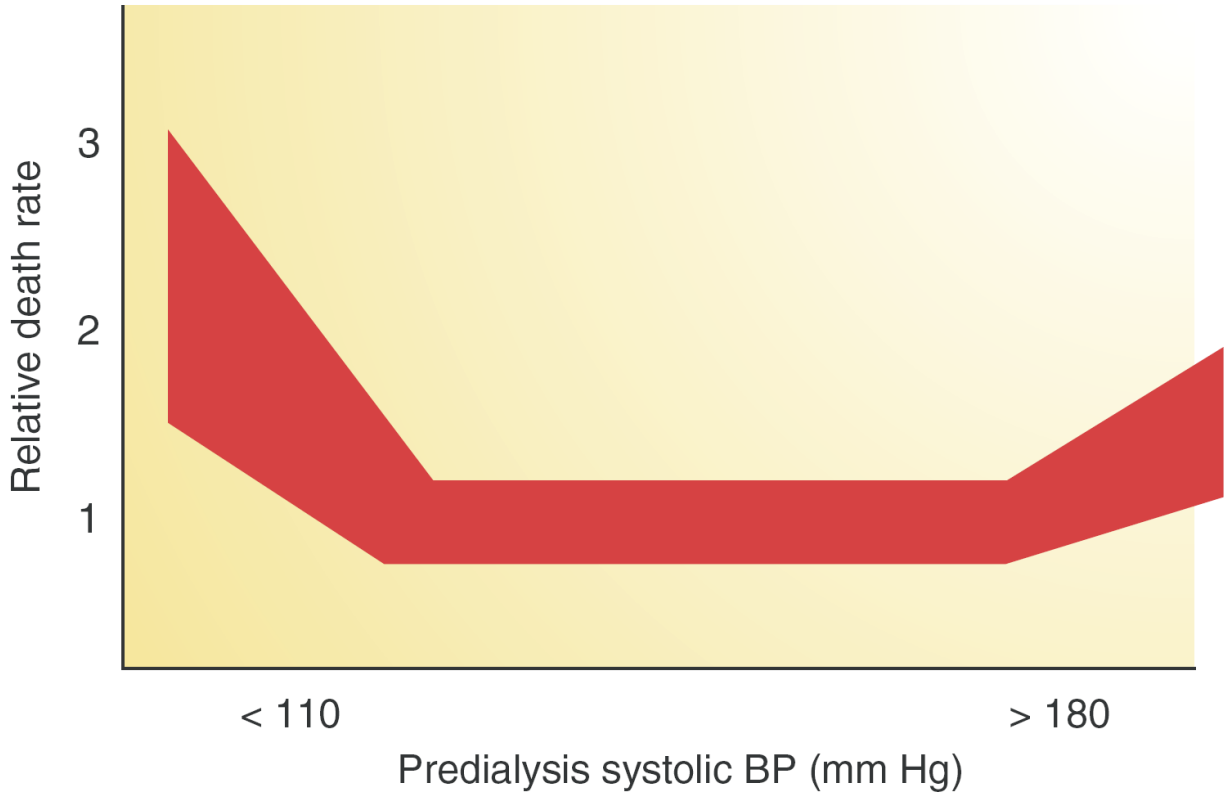
Kalantar-Zadeh et al. Hypertension 2005;45:811-817

Unadjusted survival by baseline predialysis systolic BP



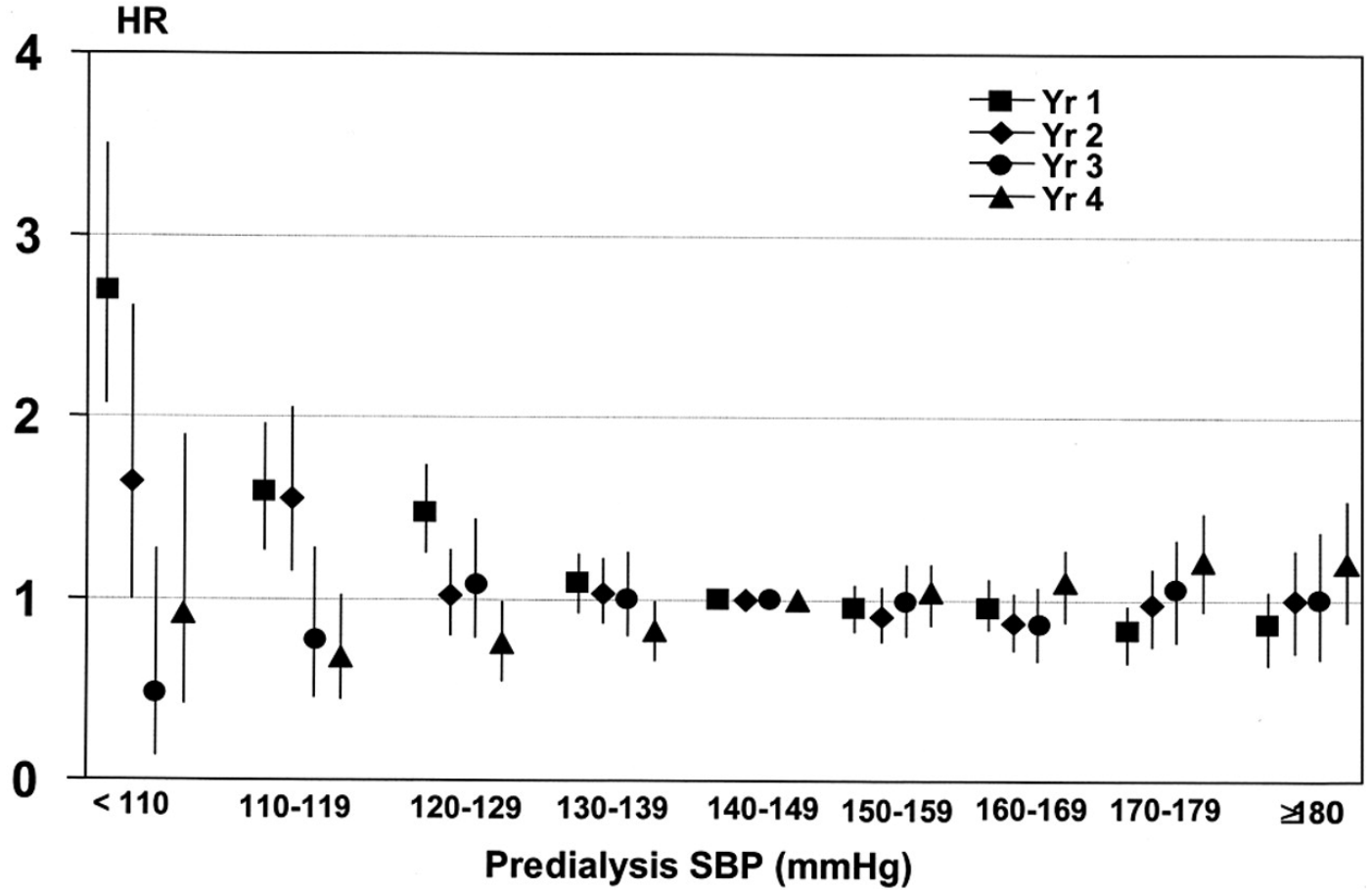
Stidley et al. J Am Soc Nephrol 2006;17:513-520

Relationship between blood pressure and mortality in dialysis patients.



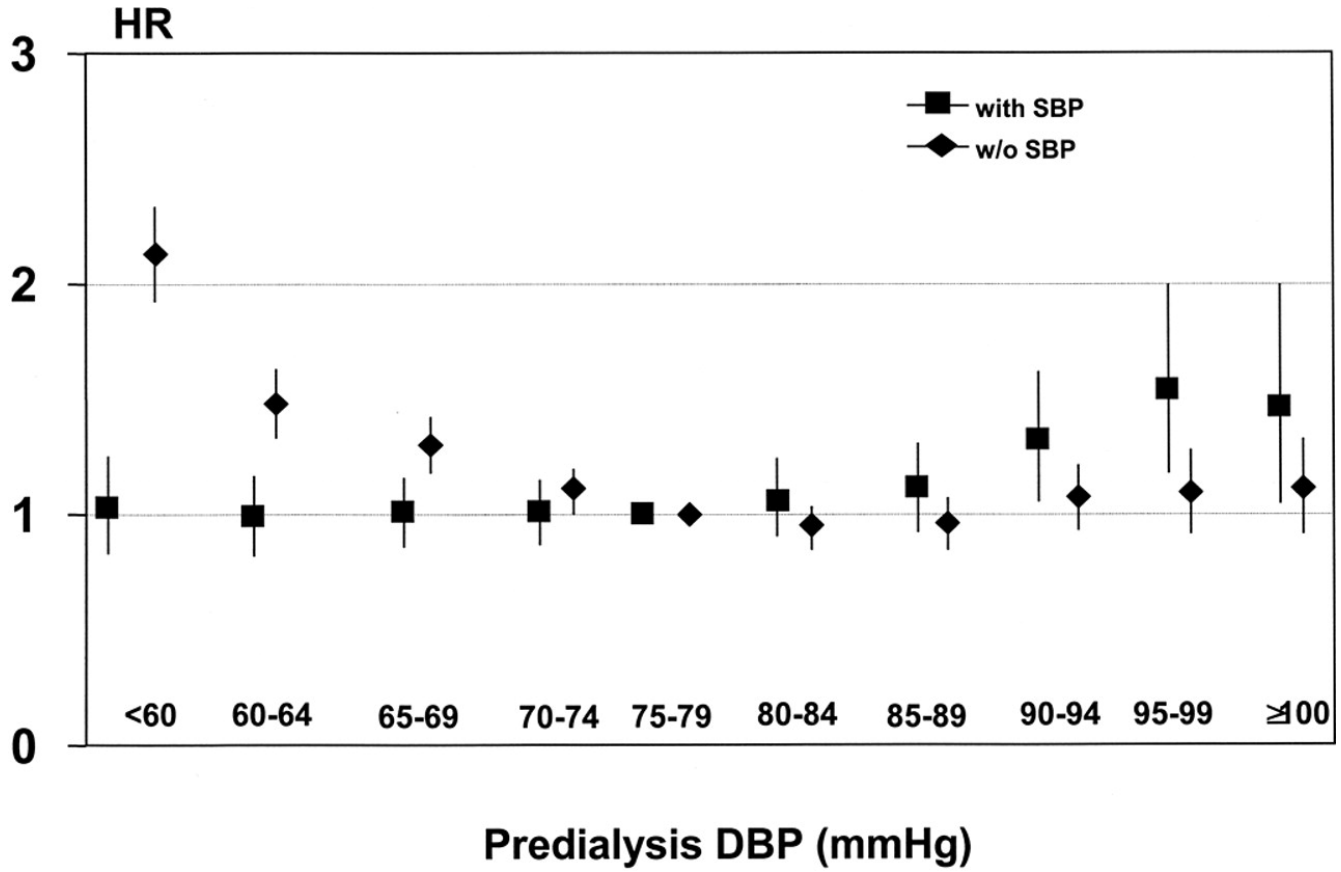
Luther JM Kidn Int 2008;73:667-668

Hazard ratios (HR) for all-cause (AC) mortality by baseline predialysis SBP



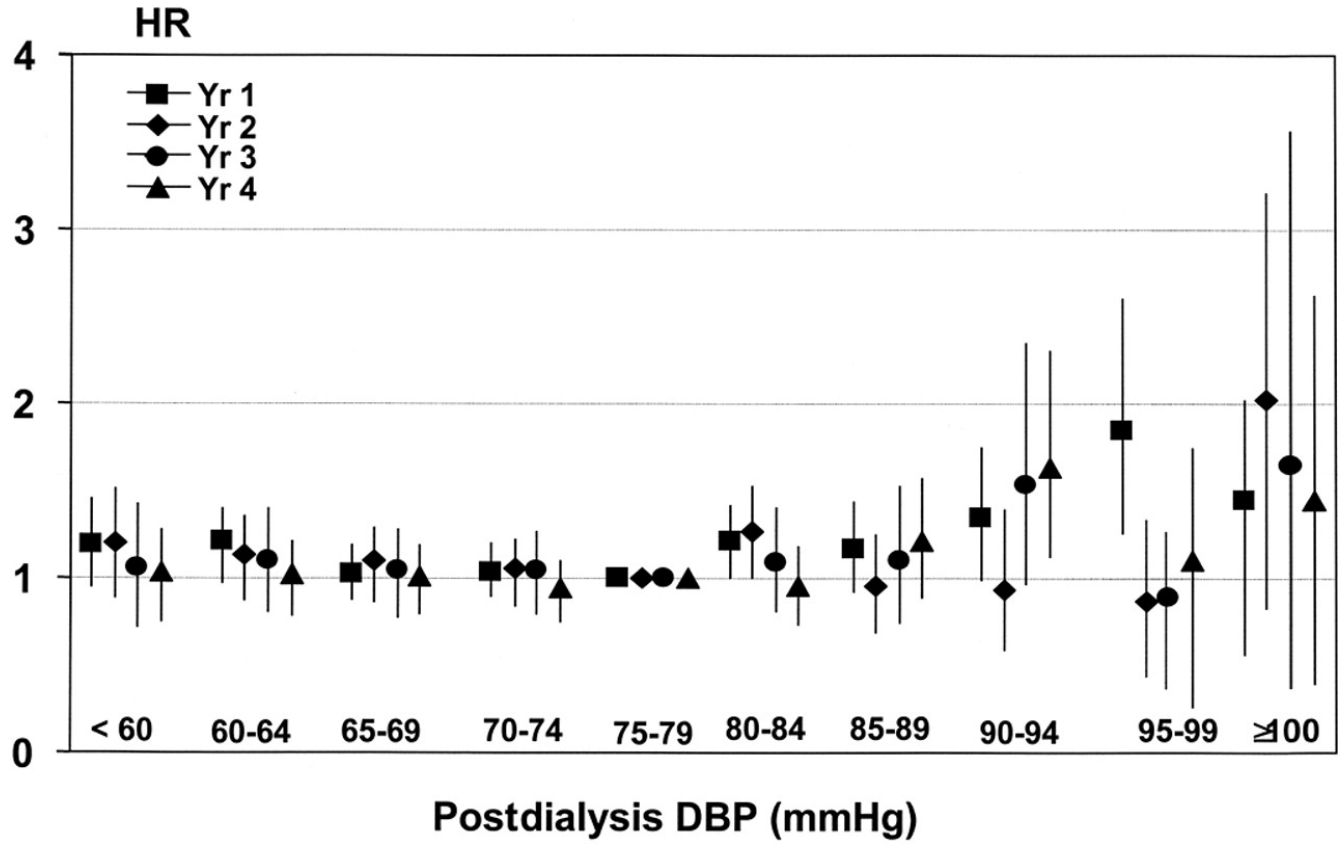
Stidley et al. J Am Soc Nephrol 2006;17:513-520

Hazard ratios (HR) for all-cause (AC) mortality by baseline predialysis DBP



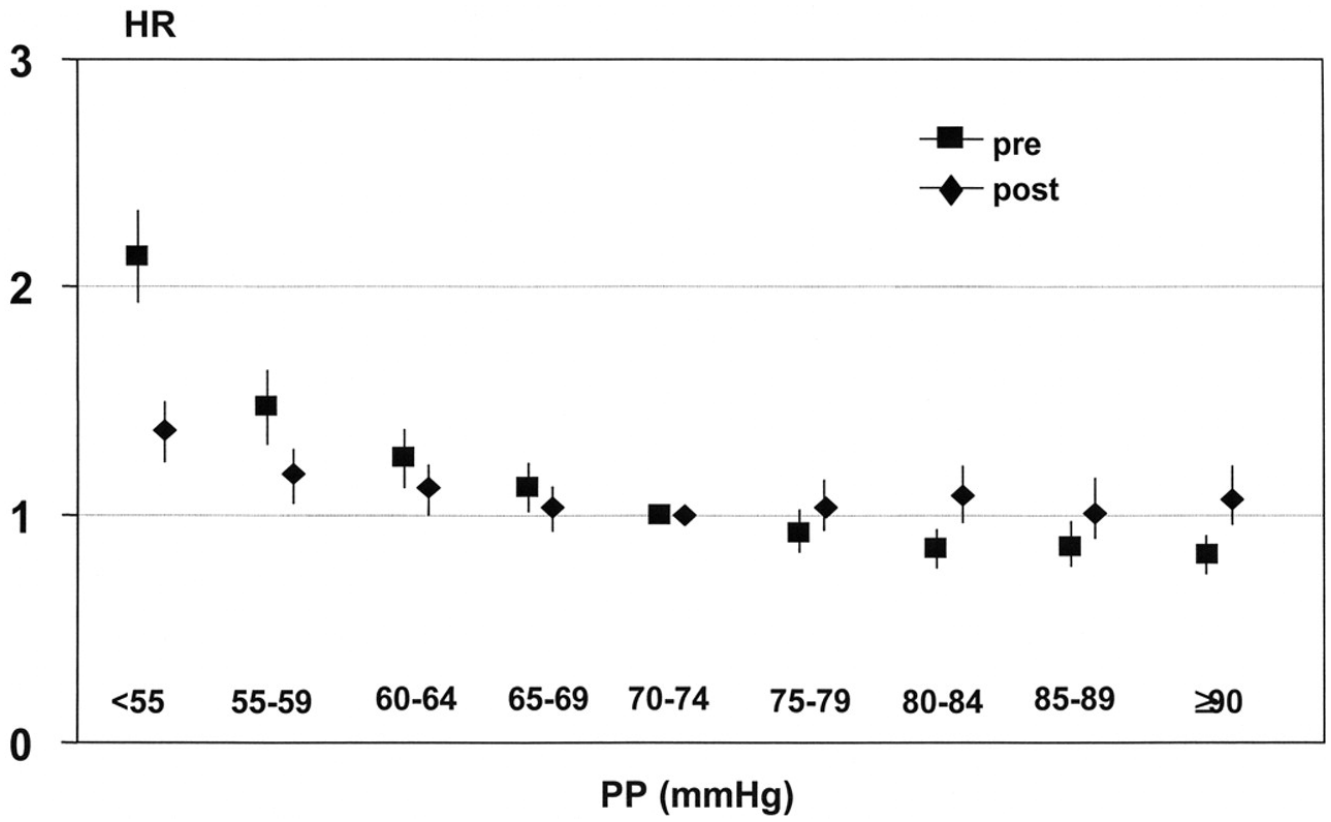
Stidley et al. J Am Soc Nephrol 2006;17:513-520

Hazard ratios (HR) for all-cause (AC) mortality by baseline postdialysis SBP



Stidley et al. J Am Soc Nephrol 2006;17:513-520

Hazard ratios (HR) for all-cause (AC) mortality by baseline pulse pressure



Stidley et al. J Am Soc Nephrol 2006;17:513-520

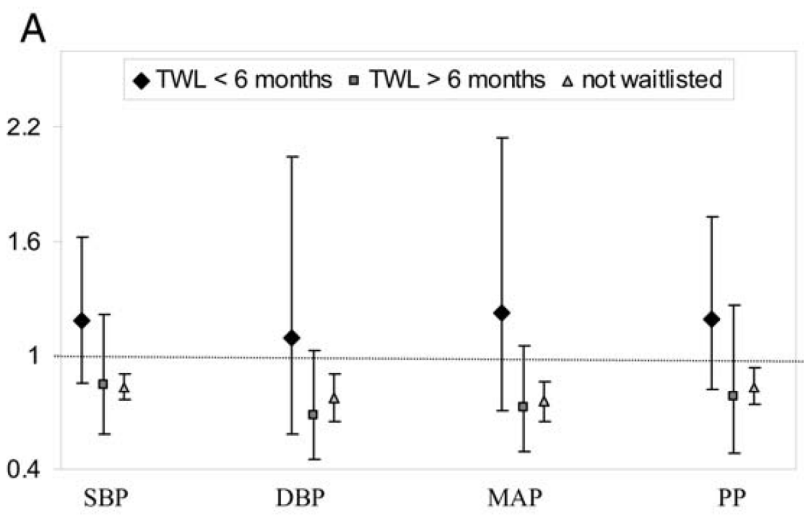
Blood pressure and mortality risk in peritoneal dialysis

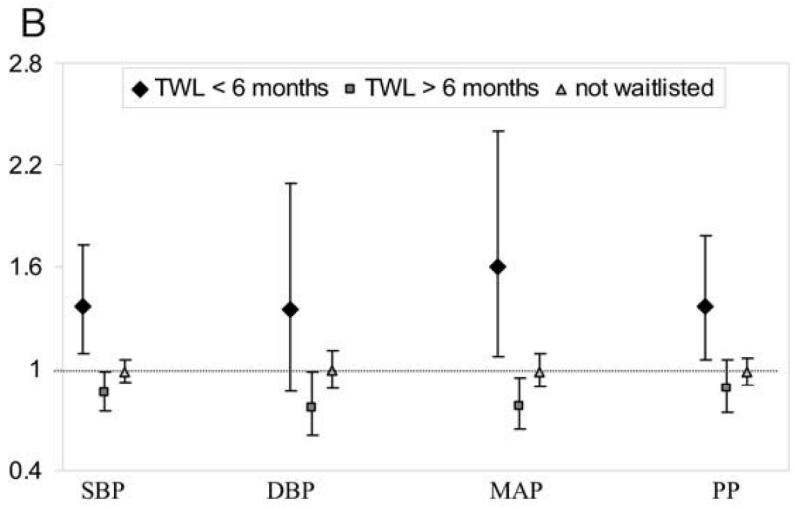
Time-Stratified Cox Proportional Hazards Model for Components of BP

		Unadjusted Model		Fully Adjusted Model*			
Time From Start of RRT	No. of Patients	RH† (95% CI)	*P*	RH† (95% CI)	*P*	*P* for BP and TWL Status Interaction‡	*P* for BP and Diabetes Interaction‡
Systolic BP							
180 d-1 y	2,770	0.88 (0.80-0.96)	0.002	0.84 (0.78-0.92)	<0.001	0.04	0.3
Years 2-3	2,642	1.02 (0.98-1.06)	0.4	0.97 (0.93-1.01)	0.2	0.2	0.1
Years 4-5	1,729	1.06 (1.00-1.12)	0.05	0.98 (0.92-1.03)	0.4	0.003	0.02
Years 6+	911	1.14 (1.05-1.23)	0.001	1.10 (1.01-1.19)	0.03	0.5	0.03
Diastolic BP							
180 d-1 y	2,770	0.68 (0.59-0.79)	<0.001	0.78 (0.67-0.91)	0.001	0.3	0.6
Years 2-3	2,642	0.82 (0.76-0.88)	<0.001	0.94 (0.88-1.02)	0.1	0.3	0.2
Years 4-5	1,729	0.82 (0.74-0.91)	<0.001	0.96 (0.87-1.07)	0.5	0.04	0.1
Years 6+	911	0.89 (0.78-1.02)	0.1	0.97 (0.84-1.12)	0.6	0.4	0.1
Mean arterial pressure							
180 d-1 y	2,770	0.73 (0.64-0.84)	<0.001	0.77 (0.67-0.87)	<0.001	0.1	0.8
Years 2-3	2,642	0.91 (0.86-0.97)	0.004	0.95 (0.89-1.01)	0.1	0.2	0.1
Years 4-5	1,729	0.94 (0.86-1.03)	0.1	0.96 (0.88-1.05)	0.4	0.005	0.05
Years 6+	911	1.03 (0.92-1.17)	0.6	1.05 (0.93-1.20)	0.4	0.4	0.03
Pulse pressure							
180 d-1 y	2,770	1.00 (0.90-1.11)	0.9	0.85 (0.76-0.95)	0.003	0.1	0.2
Years 2-3	2,642	1.14 (1.08-1.19)	<0.001	0.98 (0.93-1.03)	0.4	0.3	0.4
Years 4-5	1,729	1.19 (1.12-1.27)	<0.001	0.98 (0.91-1.06)	0.6	0.03	0.1
Years 6+	911	1.29 (1.18-1.41)	<0.001	1.18 (1.06-1.31)	0.002	0.8	0.1

Udayaraj et al. AJKD 2009;53:70-78

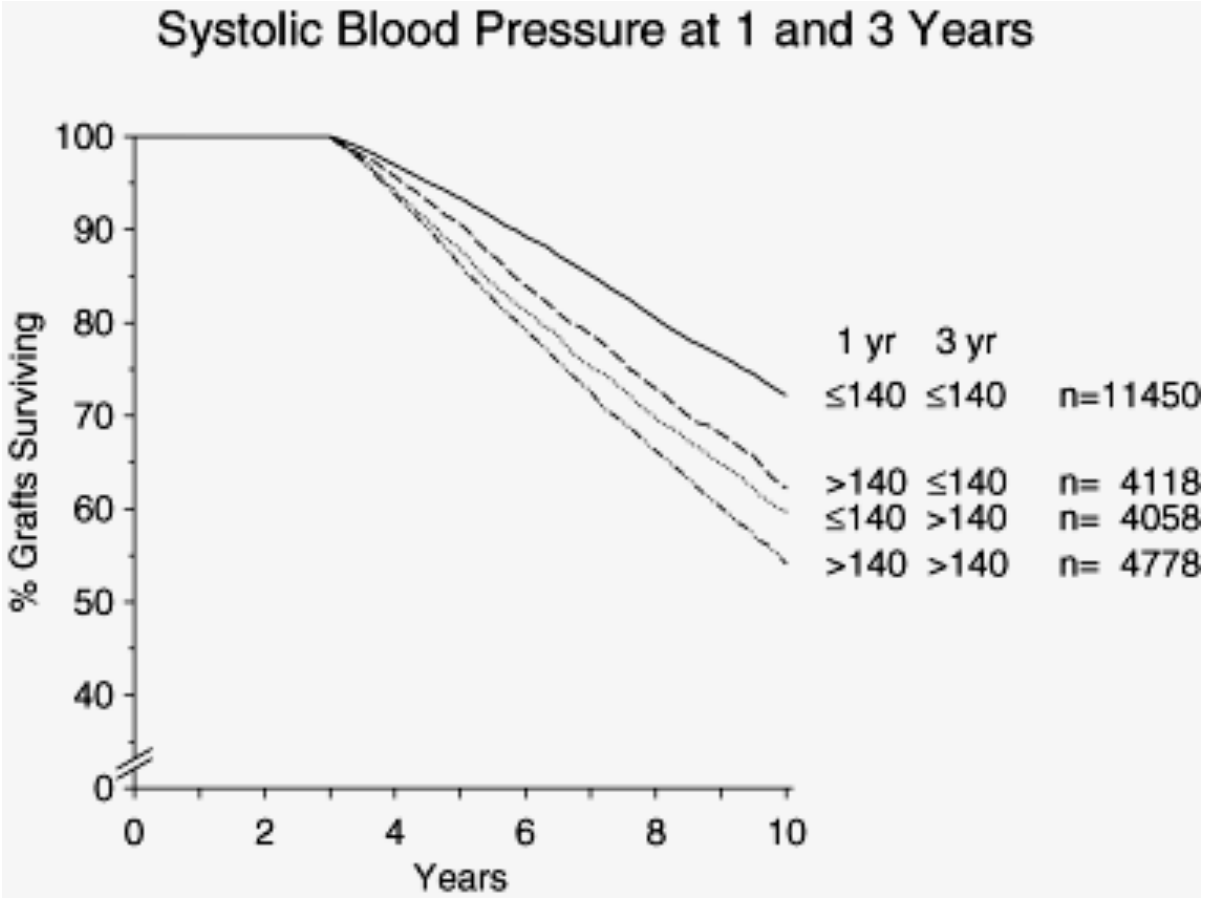
Blood Pressure and mortality risk in PD Patients





Udayaraj et al. AJKD 2009;53:70-78

Blood Pressure and mortality risk in transplanted patients



Opelz et al. Am J Transplant 2005; 5: 2725

Beta blockers in the management of chronic kidney disease

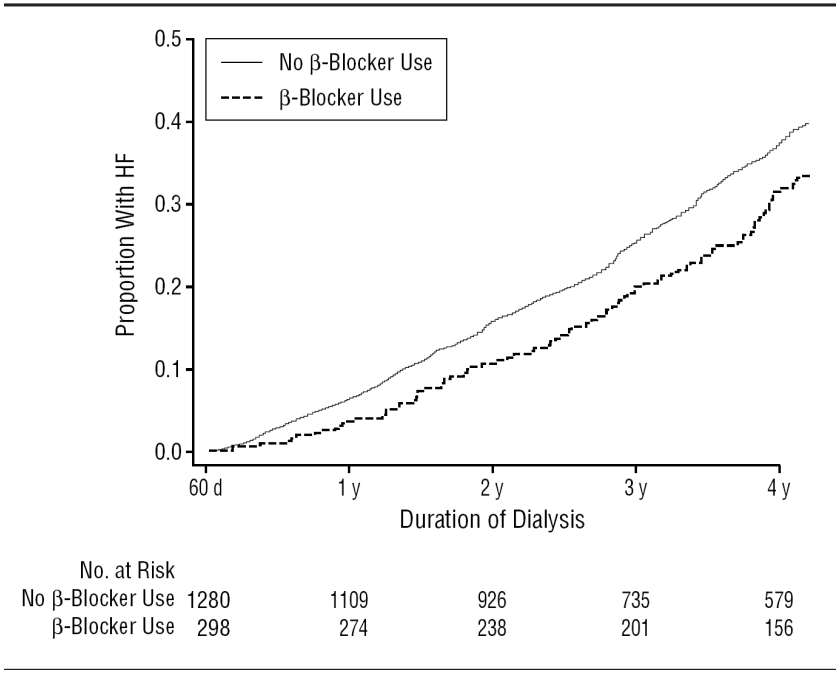
- Increased sympathetic activity in patients with moderate renal failure as well as in ESRD. Level of sympathetic activity is an independent predictor of total and cardiovascular mortality in patients with ESRD.

- Coronary heart disease and heart failure (HF) are the most common causes of death in these patients.

Observational studies of beta blockers

(Analyses of the Dialysis Morbidity and Mortality Studies DMMS conducted by the US Renal Data System)

- 2550 pts observed 60 days after dialysis
- In patients WITHOUT a history of HF, use of beta blockers was associated with lower subsequent risk of de novo HF, combined HF and cardiac death and all cause death.
- Beta-blockers were used by only 20% of patients in this cohort regardless of the presence of previous HF.



Abbott et al. Arch Intern Med 2004;164:2465-2471

Observational studies of beta blockers

beta blockers and mortality -USRDS Waves 3 and 4 Study

	Unadjusted HR	Adjusted HR
Calcium channel antagonists[d]	0.95 (0.90, 1.00) $P = 0.04$	1.0 (0.94, 1.07) $P = 0.9$
Angiotensin-converting enzyme inhibitors[d]	0.94 (0.88, 1.01) $P = 0.07$	1.05 (0.96, 1.17) $P = 0.3$
Beta blockers[d]	0.72 (0.66, 0.79) $P < 0.0001$	0.84 (0.75, 0.93) $P = 0.001$
Alpha blockers[d]	0.87 (0.77, 1.00) $P = 0.05$	0.93 (0.80, 1.09) $P = 0.4$
Centrally active agents[d]	0.89 (0.82, 0.96) $P = 0.004$	4 (0.97, 1.17) $P = 0.2$
Vasodilators[d]	0.73 (0.65, 0.82) $P < 0.0001$	0.99 (0.86, 1.14) $P = 0.9$

ONLY 8.5% of dialysis patients were treated with beta blockers !

Foley et al. Kidney International 2002;62:1784-1790

Observational studies of beta blockers

Predictors of survival after cardiac arrest in outpatient hemodialysis clinics (after 24hours and after 6 months)

ACE inhibitor or ARB	152 (39.0)	142 (48.0)	0.02
BBL	156 (40.0)	157 (53.0)	0.0007
statin	119 (30.5)	88 (29.7)	0.82
ASA	142 (36.4)	112 (37.8)	0.70
CCB	126 (32.3)	116 (39.2)	0.06
other antiarrhythmic	99 (25.4)	95 (32.1)	0.05

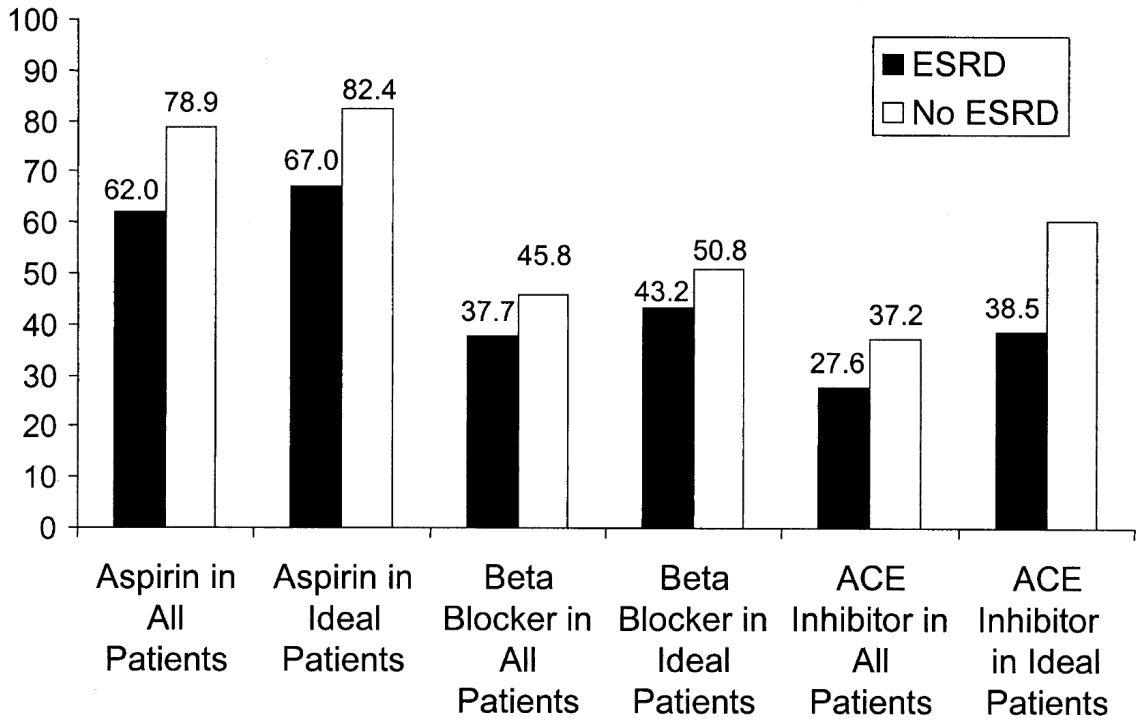
ACE inhibitor or ARB	238 (39.1)	56 (72.7)	<0.0001
BBL	256 (42.0)	57 (74.0)	<0.0001
statin	175 (28.7)	32 (41.6)	0.02
aspirin	213 (35.0)	41 (53.2)	0.002
CCB	197 (32.3)	45 (58.4)	<0.0001
other antiarrhythmic	161 (26.4)	33 (42.9)	0.003

Pun et al. CJASN 2007;2: 491-500

Observational studies of beta blockers

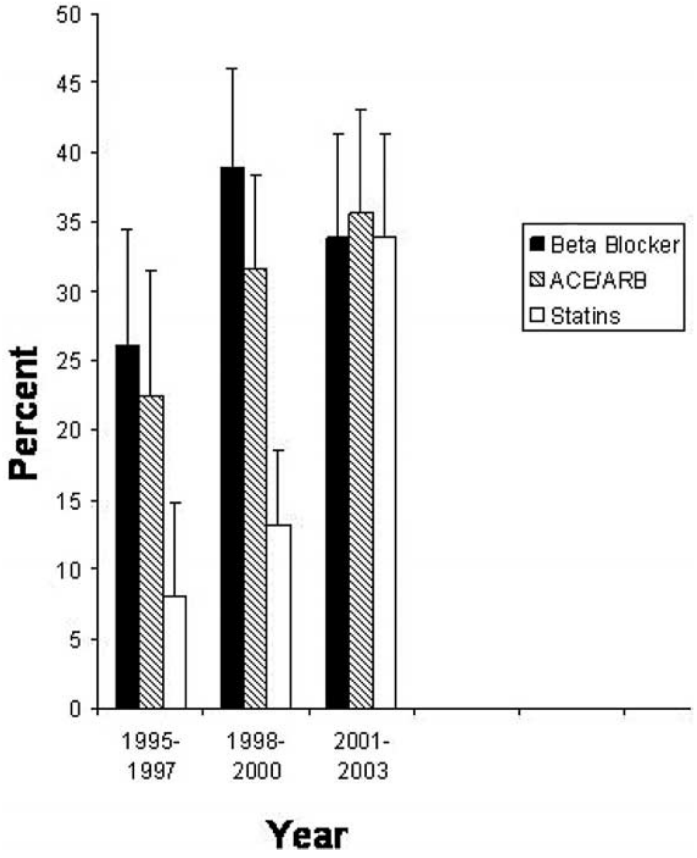
ESRD Database + Cooperative Cardiovascular Project Database

Association of medication classes with 30-day mortality after Myocardial infarction in pts with ESRD



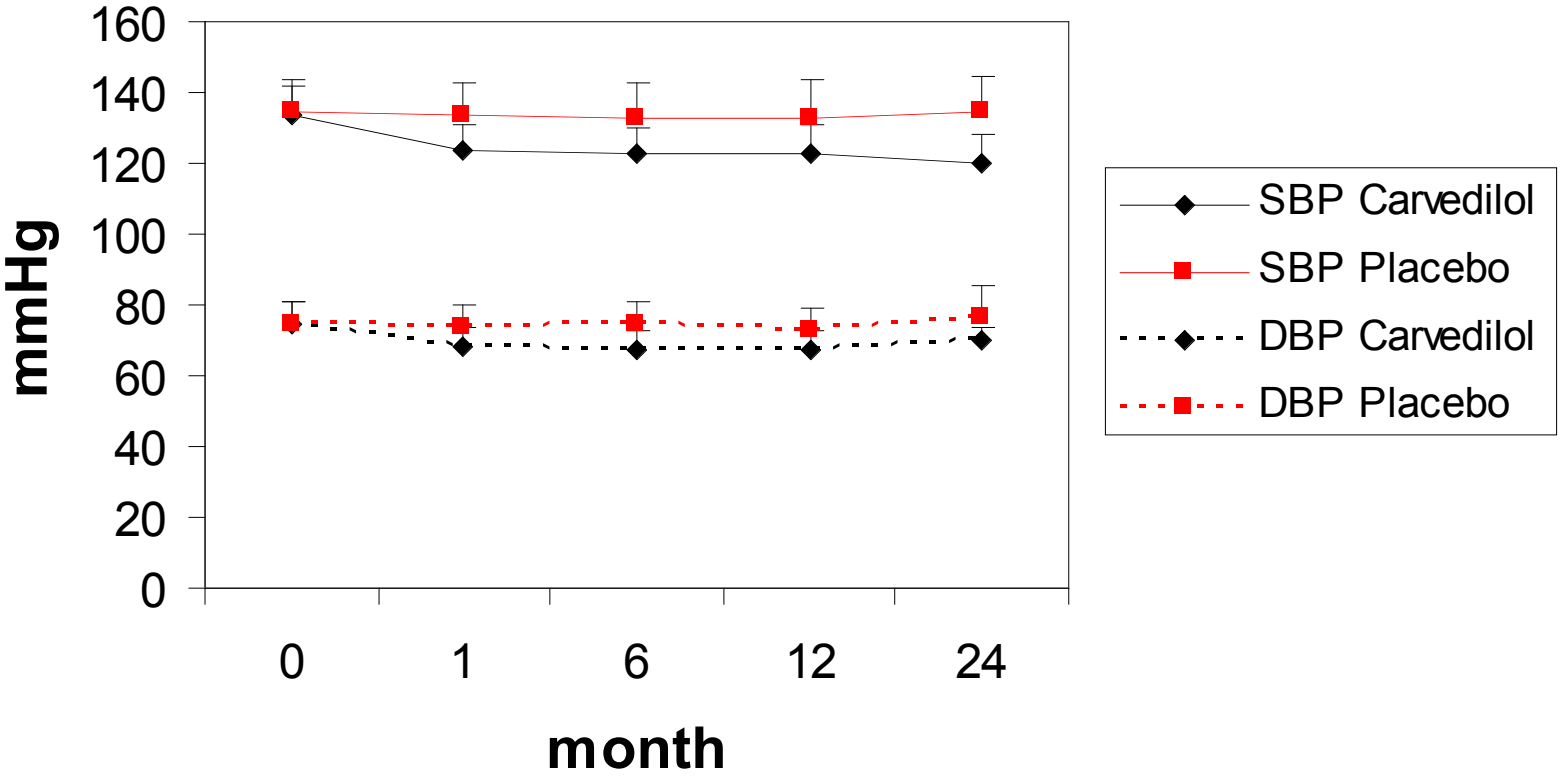
Berger et al. JACC 2003;42:201-208

Poor short-term survival and low use of cardiovascular medications in elderly dialysis patients after acute myocardial infarction,



Winkelmeyer et al AJKD 2005;47:301-308

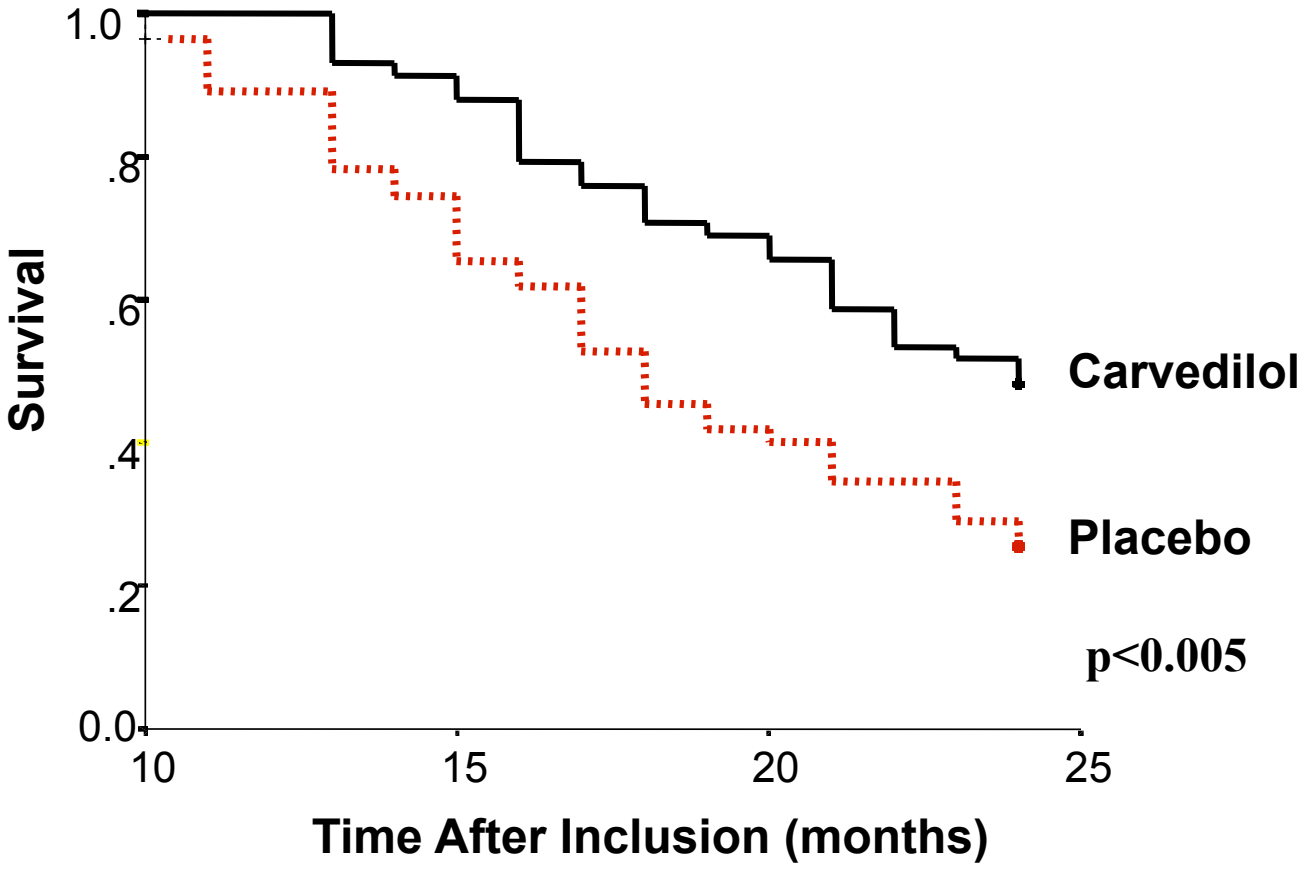
Carvedilol increases two year survival in dialysis patients with dilated cardiomyopathy



Cice et al. JACC 2003; 41:1438-1444

Carvedilol in patients on hemodialysis

Impact on all cause mortality

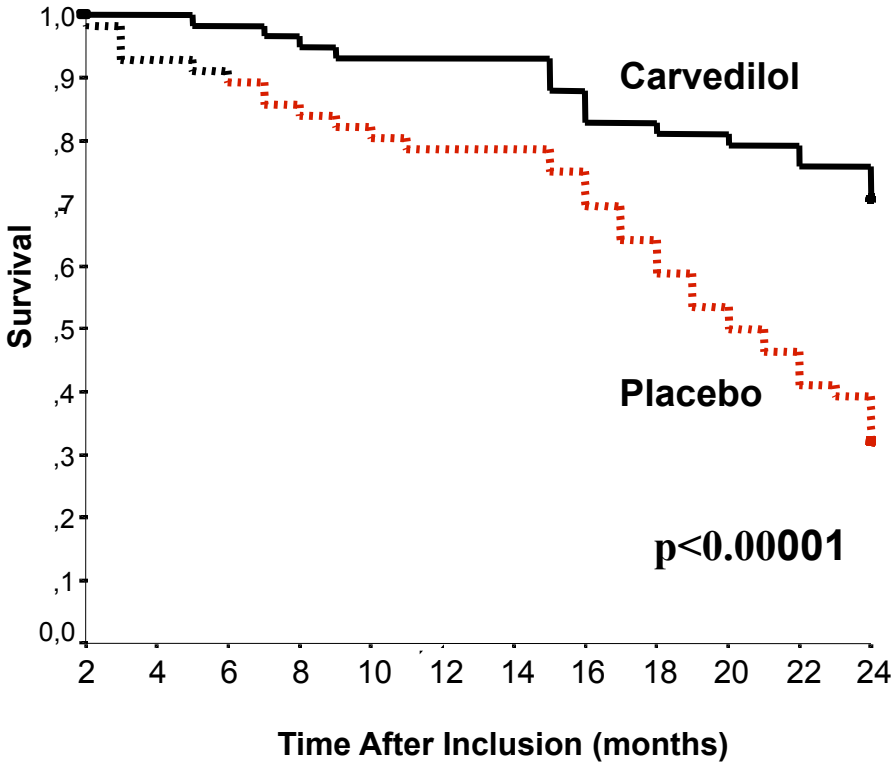


Cice et al. JACC 2003; 41:1438-1444

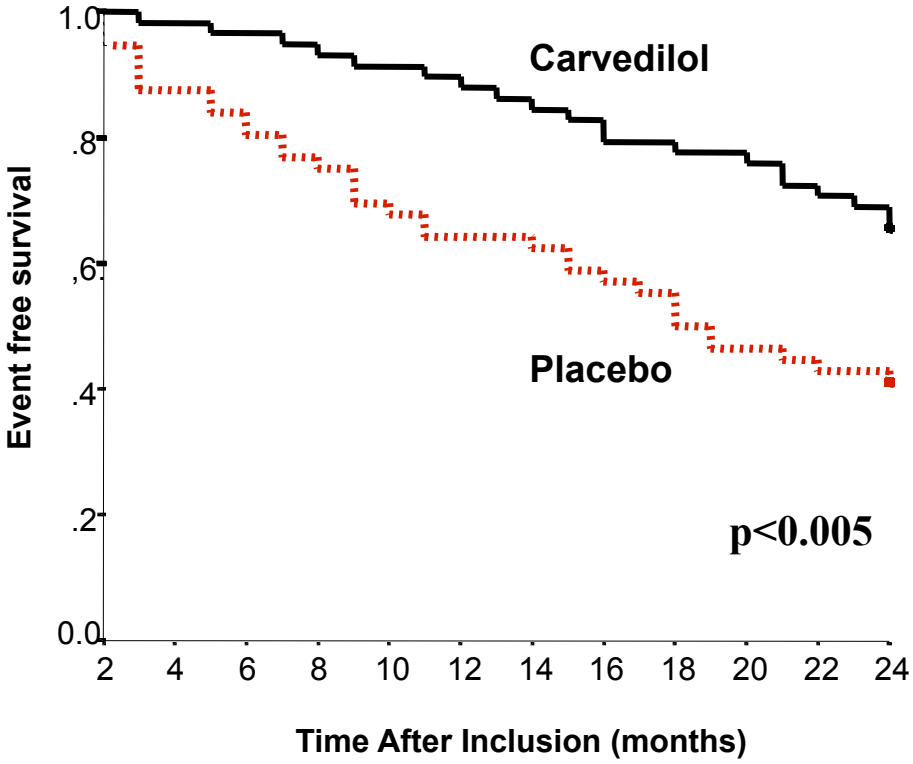
Carvedilol in patients on hemodialysis

Cardiovascular mortality and all cause hospitalization

CARDIOVASCULAR MORTALITY



EVENT-FREE SURVIVAL



Cice et al. JACC 2003; 41:1438-1444

RAS Inhibitors in patients on HD

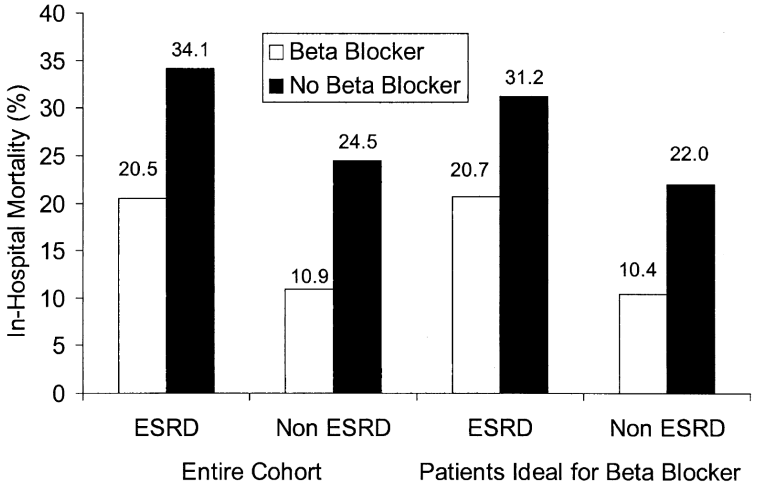
Studies focusing on end-organ damage

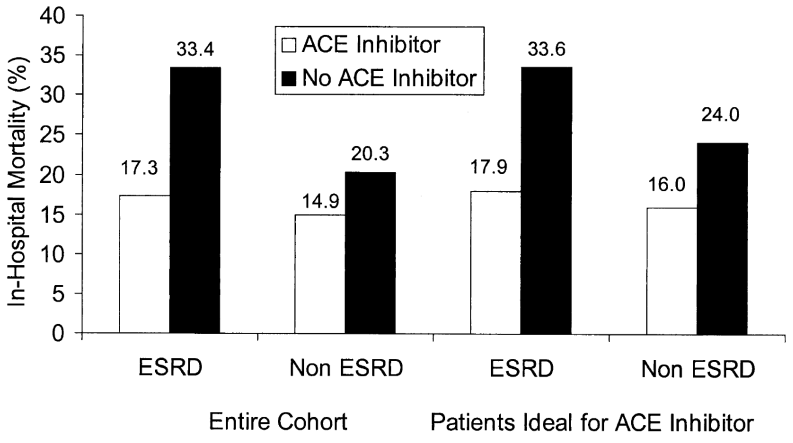
1. A 12-month treatment with ramipril did not cause significant regression of left ventricular hypertrophy in **46** normotensive hemodialysis patients (*Wen-Chung Yu et al. AJKD 2006;47:478-484*)
2. Valsartan (in combination with amlodipine) reduced markers of oxidative stress in **30** pts on HD (*Aslam et al. Kidney International 2006;70:2109-2115*)
3. Losartan and tandolapril improved arterial stiffness in **64** pts on HD (*Ichihara et al. AJKD 2005;45:866-874*)
4. Enalapril and Losartan lead to regression of LVH in **33** incident hemodialysis patients (*Suzuki et al. Ther Apheresis and Dialysis 2004;4:320-327*)

ACE inhibitors after cardiac events in patients on HD

ESRD Database + Cooperative Cardiovascular Project Database

Association of medication classes with 30-day mortality after Myocardial infarction in pts with ESRD

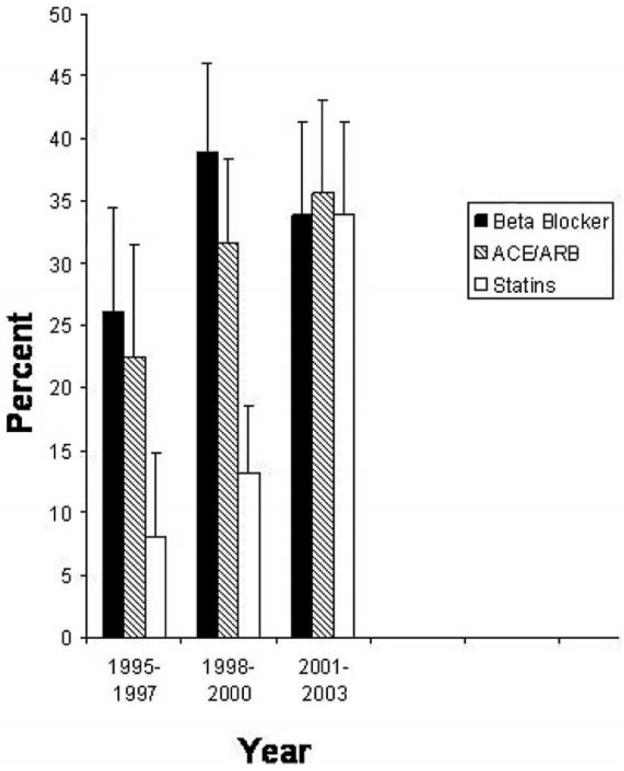




Berger et al. JACC 2003;42:201-208

ACE Inhibitors after cardiac events in patients on Hemodialysis

- Congestive heart failure was present in 80% of the study cohort
- ACE inhibitors were used in only 30% of the patients
- 1 year mortality rate was very high (63%)
- Use of ACE I or ARB was associated with a 30% reduction in 1year mortality



Winkelmeyer et al AJKD 2005;47:301-308

Fosinopril in Dialysis (FOSIDIAL)Study

- The composite cardiovascular event rate was 32.7% during the 2yr follow up period

- In the intention to treat analysis there was no significant difference in the primary end point between the two groups (RR=0.93; 95%CI 0.68 to 1.26; P=0.35)

	Placebo (*N*=201)	Fosinopril (*N*=196)	*P*-value
Age (years)	67 (8)	67 (8)	0.72
Pre-dialysis BMI	27 (6)	26 (5)	0.02
Baseline SBP (mm Hg)	145 (20)	146 (19)	0.48
Baseline DBP (mm Hg)	77 (11)	77 (11)	0.74
2-week SBP (mm Hg)	148 (21)	147 (22)	0.63
2-week DBP (mm Hg)	78 (12)	77 (12)	0.57
Pulse pressure (mm Hg)	70 (17)	70 (17)	0.79
LV mass index[a]	169 (52)	179 (54)	0.001
Female	99 (49)	90 (46)	0.51
Coronary artery disease history	21 (10)	32 (16)	0.05
Peripheral artery disease history	28 (14)	35 (18)	0.26
Stroke history	11 (6)	18 (9)	0.1
Smoking	22 (11)	24 (12)	0.68
Diabetes	56 (28)	68 (35)	0.12
Dyslipidemia	73 (36)	83 (42)	0.21
Residual diuresis (ml/day)	308 (412)	232 (329)	0.07
Duration of renal replacement therapy (years)	4.4 (4.7)	5.3 (6)	0.04
Duration of dialysis (years)	3.8 (4)	4.4 (5)	0.11
Kt/V	1.3 (0.3)	1.4 (0.5)	0.08
Interdialytic weight change (kg)	2.4 (1)	2.3 (1)	0.22
Study drug treatment duration (days)	541 (269)	537 (271)	0.87
HDL (mmol/l)[b]	1.1 (0.3)	1.1 (0.3)	0.71
LDL (mmol/l)[b]	3.1 (1)	3.1 (1)	0.87
C-reactive protein (mg/l)	13.1 (19.7)	12.5 (17.8)	0.76
Erythropoeitin	156 (78)	157 (80)	0.56
Oral anti-diabetic therapy	3 (2)	12 (6)	<0.001
Insulin	41 (20)	40 (20)	0.99
Lipid-lowering therapy	49 (24)	51 (26)	0.7
Antihypertensive therapy	103 (51)	107 (55)	0.51
Prior transplantation	11 (6)	18 (9)	0.1

Zannad et al. Kidney International 2006;70:1318-1324

Fosinopril in Dialysis (FOSIDIAL)Study

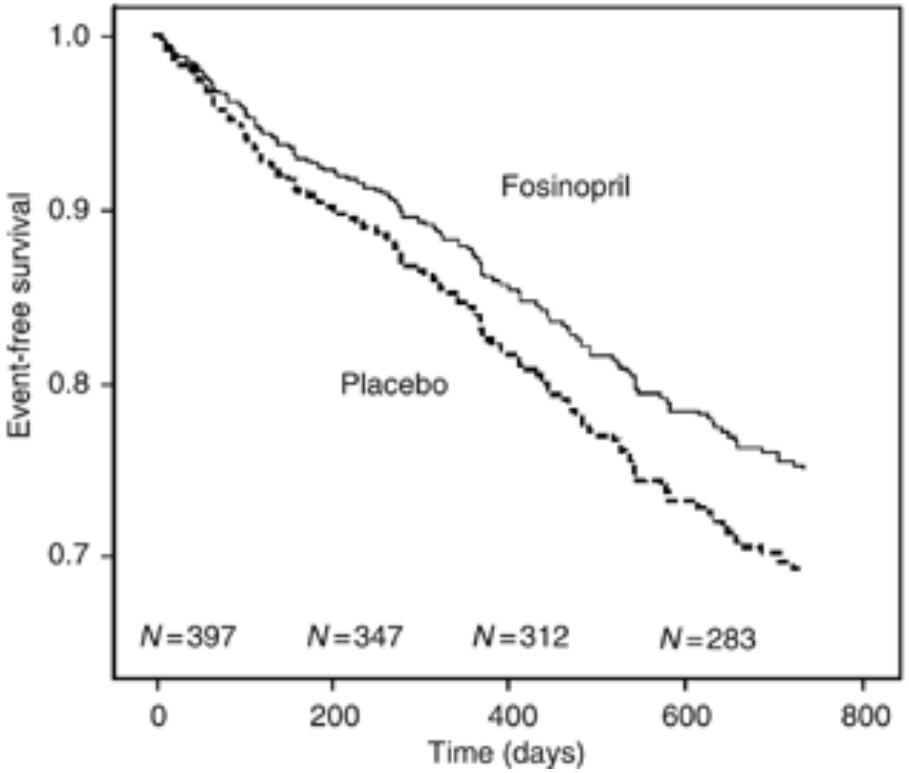
(change in SBP and DBP)

	Placebo	Fosinopril	Difference (95% CI)	*P*-value (ANCOVA)
Normotensive patients (n=159)				
Change in SBP	5.3 (14.2)	5.1 (11.9)	−0.23 (−4.6, 4.1)	0.91
Change in DBP	1.2 (7.4)	1.2 (7.9)	−0.03 (−2.3, 2.2)	0.98
Hypertensive patients (n=238)				
Change in SBP	−5.4 (15.4)	−11.7 (13.4)	−6.3 (−10.3, −2.4)	0.002
Change in DBP	−2.1 (9.1)	−4.9 (9.7)	−2.8 (−5.1, −0.5)	0.01
Response proportion (<140/90 and no DBP value <50 mm Hg)				
Normotensive	65% (84)	71% (75)	RR 1.08 (0.87–1.33)	0.49
Hypertensive	19% (117)	35% (121)	RR 1.85 (1.18–2.89)	0.008

ANCOVA, analysis of covariance; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Zannad et al. Kidney International 2006;70:1318-1324

Fosinopril in Dialysis (FOSIDIAL)Study



Zannad et al. Kidney International 2006;70:1318-1324

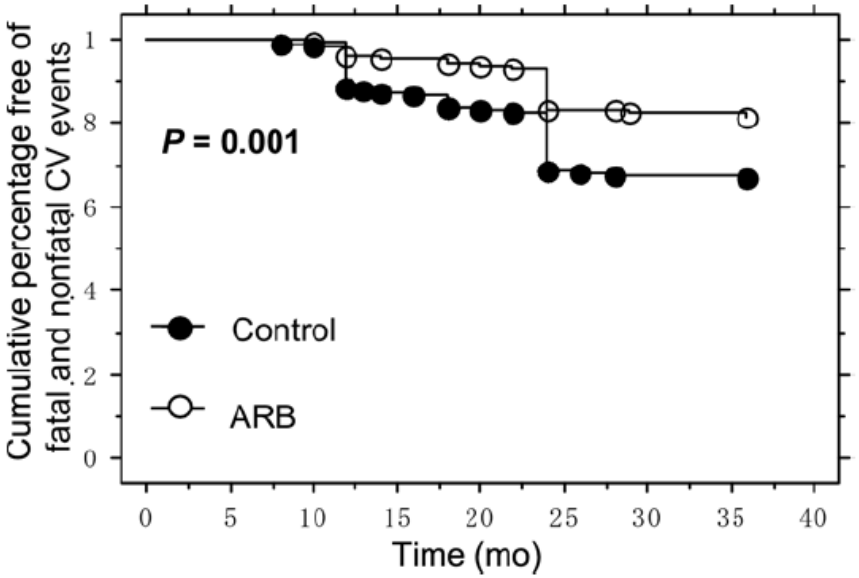
Angiotensin Receptor Blockers on Cardiovascular Events in Patients undergoing Hemodialysis

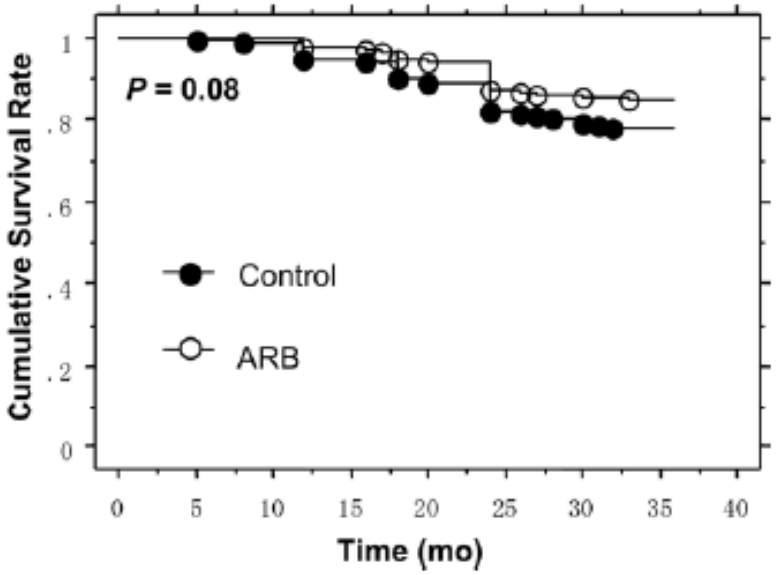
	Baseline		Year 1		Year 2		Year 3	
	ARB (n = 183)	Control (n = 183)	ARB (n = 175)	Control (n = 161)	ARB (n = 141)	Control (n = 115)	ARB (n = 134)	Control (n = 105)
SBP (mm Hg)	154 ± 20	156 ± 21	144 ± 16	144 ± 18	142 ± 14	142 ± 15	140 ± 12	140 ± 11
DBP (mm Hg)	81 ± 12	82 ± 13	80 ± 11	80 ± 10	81 ± 9	80 ± 9	80 ± 8	78 ± 7
Hemoglobin (g/dL)	9.4 ± 1.7	9.4 ± 1.2	9.5 ± 1.6	9.5 ± 1.6	9.6 ± 1.7	9.6 ± 1.5	9.5 ± 1.5	9.5 ± 1.5

Note: Hemoglobin in g/L may be converted to g/dL by multiplying by 10.
Abbreviations: ARB, angiotensin receptor blocker; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Suzuki et al. AJKD 2008;52:501-506

Angiotensin Receptor Blockers on Cardiovascular Events in Patients undergoing Hemodialysis

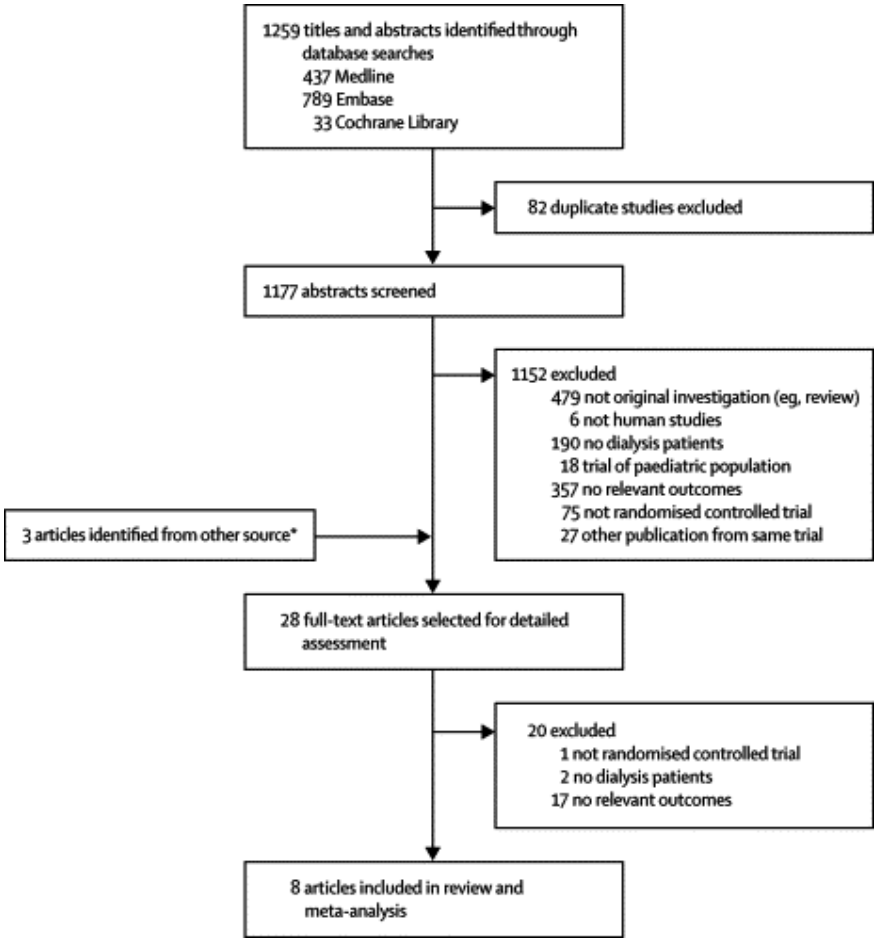




Suzuki et al. AJKD 2008;52:501-506

Effect of lowering blood pressure on cardiovascular events and mortality in patients on dialysis: a systematic review and meta-analysis of randomised controlled trials

Hiddo J Lambers Heerspink, Toshiharu Ninomiya, Sophia Zoungas, Dick de Zeeuw, Diederick E Grobbee, Meg J Jardine, Martin Gallagher, Matthew A Roberts, Alan Cass, Bruce Neal, Vlado Perkovic



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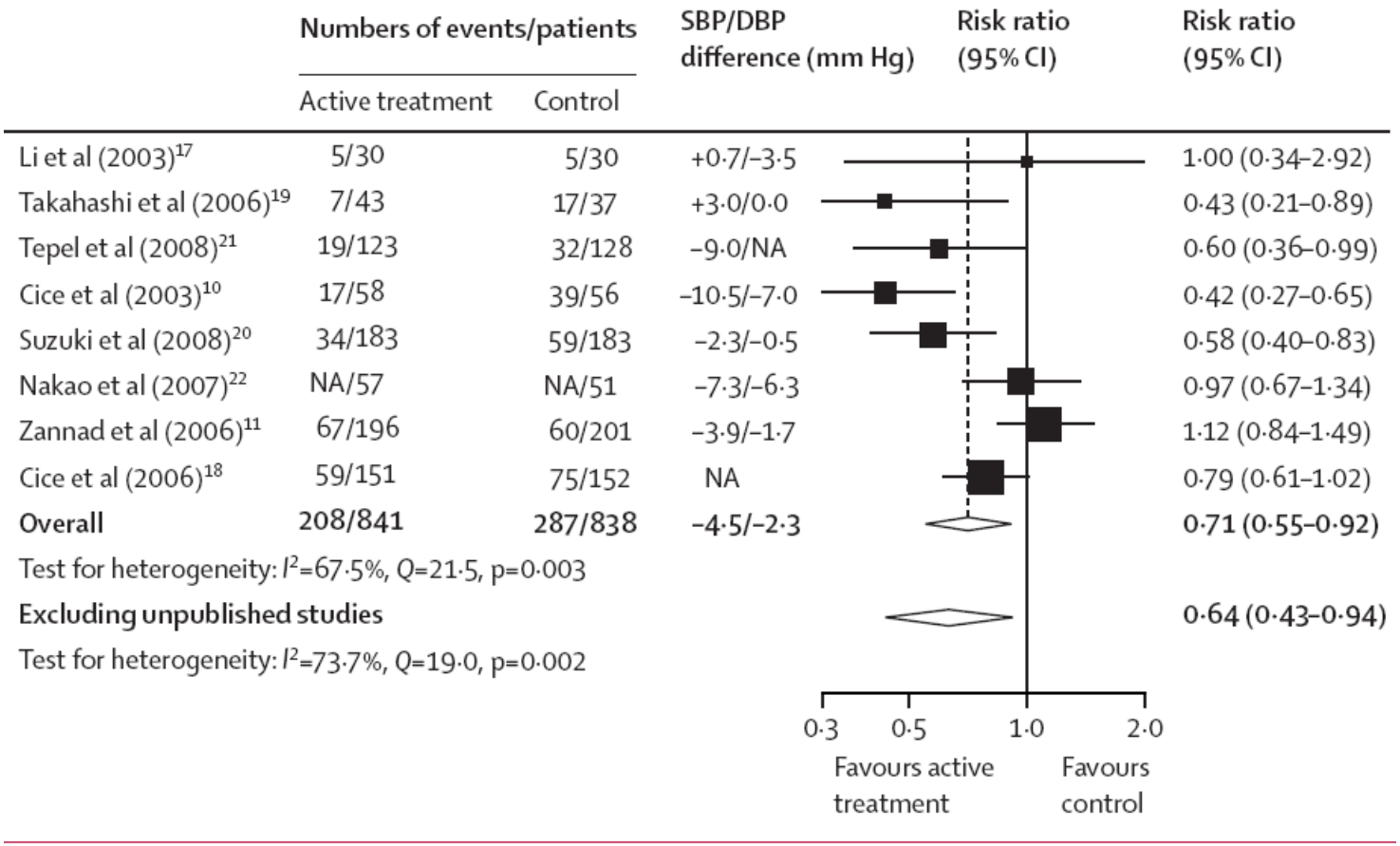
	Inclusion criteria	Active treatment	Control	Design	Cardiovascular outcome	Number of patients	Men, n (%)	Age, years (mean)	Patients with diabetes, n (%)	Number of cardiovascular events
Cice et al (2003)[10]	Uraemic patients with dilated cardiomyopathy; stable weight (<2·5 kg change before enrolment)	Carvedilol 50 mg/day	Matched placebo	Randomised, placebo-controlled, double-blind trial (unblinded for second 12 months)	Myocardial infarction, cardiovascular death	114	69 (61%)	55	NR	56
Li et al (2003)[12]	Peritoneal dialysis with residual glomerular filtration rate ≥2 mL/min /1·73 m^2; blood pressure ≥120/70 mm Hg; no ACE inhibitor/ARB use for at least 6 months before enrolment	Ramipril 5 mg/day	Conventional treatment	Randomised, open-label trial	Myocardial infarction, stroke, peripheral vascular disease, cardiovascular death	60	38 (63%)	59	28 (47%)	10
Cice et al (2006)[13]	Congestive heart failure NYHA class II and III; left ventricular ejection fraction <40%	Telmisartan 80 mg/day	Matched placebo	Randomised, placebo-controlled, double-blind trial	Cardiovascular mortality	303	158 (52%)	59	98 (32%)	134
Takahashi et al (2006)[13]	≥35 years; stable interdialytic weight; post-haemodialytic cardiothoracic ratio on chest radiograph <50% in men or 35% in women	Candesartan 16–32 mg/day	Conventional treatment	Randomised, open-label, blinded endpoint trial	Myocardial infarction, unstable angina pectoris or heart failure needing hospital admission, severe arrhythmia, sudden death	80	47 (59%)	61	26 (33%)	24
Zannad et al (2006)[11]	50–80 years; haemodialyis for at least 6 months three times a week; left ventricular hypertrophy within 3 months of enrolment	Fosinopril 20 mg/day	Matched placebo	Randomised, placebo-controlled, double-blind trial	Myocardial infarction, stroke, hospital admission for heart failure, unstable angina pectoris, revascularisation, cardiac arrest, cardiovascular death	397	208 (52%)	67	124 (31%)	127
Nakao et al (2007)[22]	Haemodialysis for at least 6 months; BNP >200 pg/mL; hANP <150 pg/mL; left ventricular hypertrophy	Carvedilol 20 mg/day	Matched placebo	Randomised, open-label, placebo-controlled trial	Myocardial infarction, stroke, hospital admission for heart failure, peripheral vascular disease, arrhythmia, cardiomyopathy, sudden cardiac arrest, cardiovascular death	108	64 (59%)	60	52 (48%)	NR
Suzuki et al (2008)[20]	30–80 years; haemodialyis for at least 12 months; systolic blood pressure >160 mm Hg or >150 mm Hg if taking antihypertensive agents	Candesartan 12 mg/day, losartan 100 mg/day, or valsartan 160 mg/day	Conventional treatment	Randomised open-label trial	Myocardial infarction, stroke, CABG, percutaneous coronary intervention, congestive heart failure, cardiovascular death	366	216 (59%)	60	187 (51%)	93
Tepel et al (2008)[21]	≥18 years; haemodialysis for at least 3 months; blood pressure ≥140/90 mm Hg	Amlodipine 10 mg/day	Matched placebo	Randomised, placebo-controlled, double-blind trial	Myocardial infarction, CABG, ischaemic stroke, peripheral vascular disease needing amputation, all-cause mortality	251	159 (63%)	61	73 (29%)	51

Risk of cardiovascular events for blood pressure lowering treatment vs control regimens



	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					

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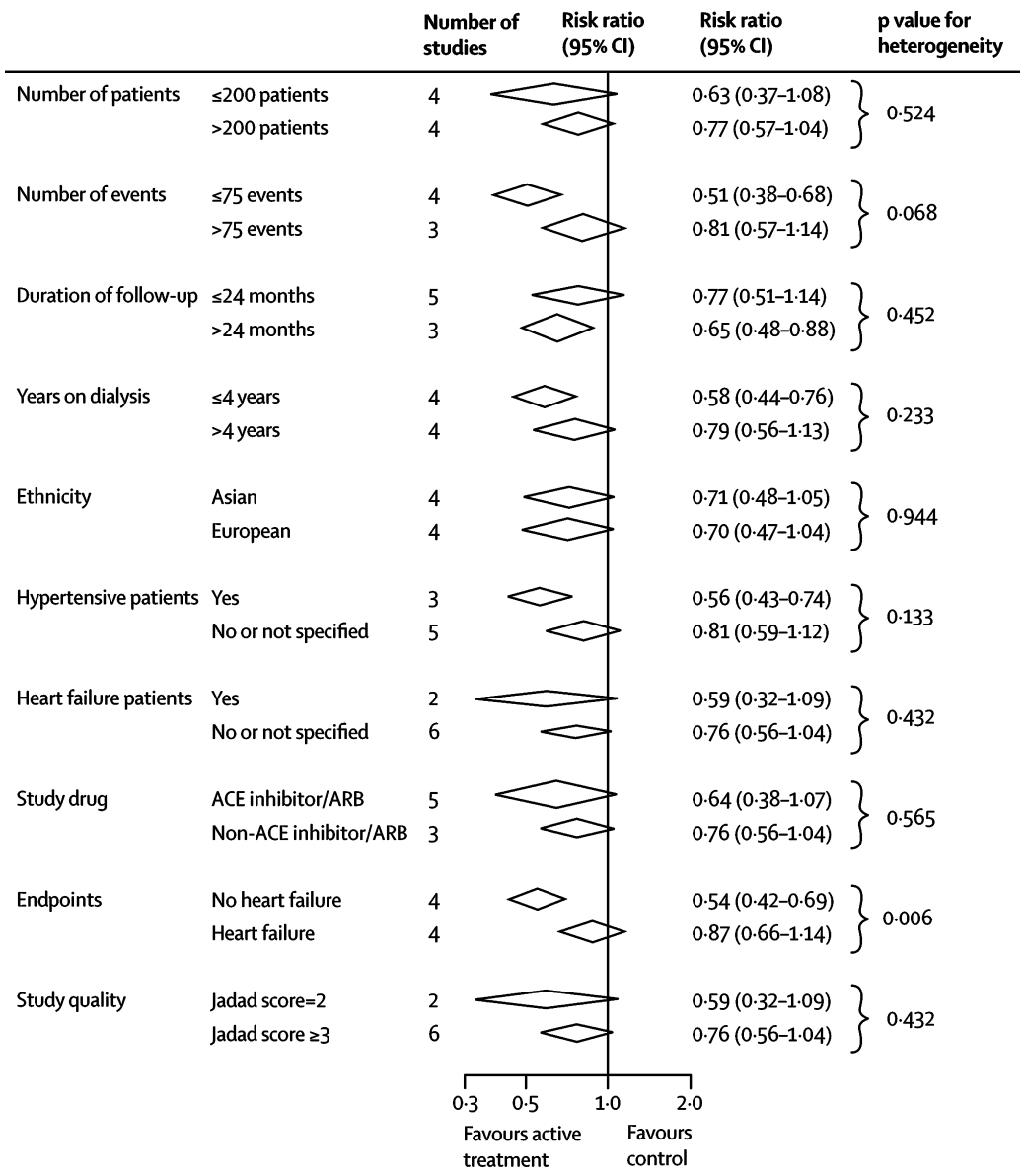
Subgroup analyses for the effects of treatment on cardiovascular events



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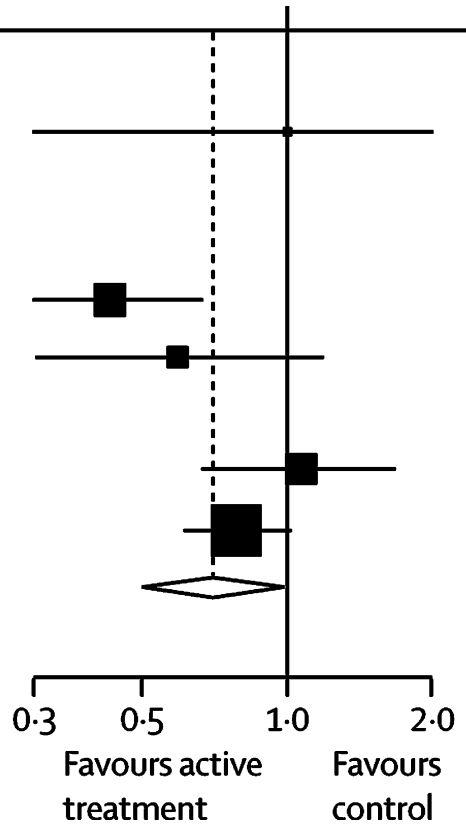
Risk of cardiovascular mortality for blood pressure lowering treatment vs control regimens

Cardiovascular mortality			
Li et al (2003)[17]	2/30	2/30	1·00 (0·15–6·64)
Takahashi et al (2006)[19]	NR	NR	..
Tepel et al (2008)[21]	NR	NR	..
Cice et al (2003)[10]	17/58	38/56	0·43 (0·28–0·67)
Suzuki et al (2008)[20]	12/183	20/183	0·60 (0·30–1·19)
Nakao et al (2007)[22]	NR	NR	..
Zannad et al (2006)[11]	31/196	30/201	1·05 (0·67–1·68)
Cice et al (2006)[18]	59/151	75/152	0·80 (0·61–1·02)
Overall	**121/618**	**165/622**	**0·71 (0·50–0·99)**

Test for heterogeneity: I^2=54·6%, Q=8·8, p=0·07



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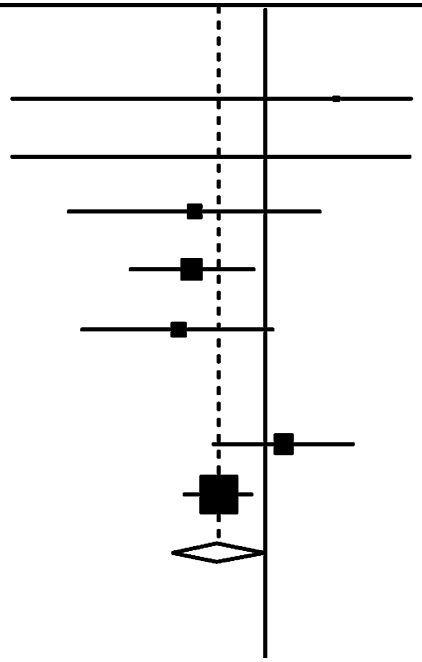
Risk of all-cause mortality for blood pressure lowering treatment vs control regimens

	Numbers of events/patients		Risk ratio (95% CI)	Risk ratio (95% CI)
	Active treatment	Control		
All-cause mortality				
Li et al (2003)[17]	3/30	2/30		1·40 (0·30–6·55)
Takahashi et al (2006)[19]	0/43	7/37		0·06 (0·00–0·97)
Tepel et al (2008)[21]	15/123	20/128		0·72 (0·39–1·30)
Cice et al (2003)[10]	30/58	41/56		0·71 (0·53–0·95)
Suzuki et al (2008)[20]	25/183	38/183		0·66 (0·41–1·04)
Nakao et al (2007)[22]	NR	NR		..
Zannad et al (2006)[11]	52/196	49/201		1·09 (0·78–1·52)
Cice et al (2006)[18]	88/151	111/152		0·80 (0·68–0·94)
Overall	**213/784**	**268/787**		**0·80 (0·66–0·96)**

Test for heterogeneity: I^2=30·0%, Q=8·57, p=0·20



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Study treatment discontinuation rates

	Active agent	Active run-in*	Excluded during run-in	Patients who discontinued therapy	
				Active treatment	Control treatment
Cice et al (2003)[10]	β blocker	Yes	18/132 (14%)	11/58 (19%)	7/56 (13%)
Li et al (2003)[17]	ACE inhibitor	No	N/A	5/30 (17%)	0/30 (0%)
Cice et al (2006)[18]	ARB	No	N/A	20/151 (13%)	16/152 (11%)
Takahashi et al (2006)[19]	ARB	NR	N/A	NR	NR
Zannad et al (2006)[11]	ACE inhibitor	Yes	6/417 (1%)	NR	NR
Nakao et al (2007)[22]	β blocker	No	N/A	NR	NR
Suzuki et al (2008)[20]	ARB	No	N/A	3/183 (2%)	3/183 (2%)
Tepel et al (2008)[21]	Calcium-channel blocker	No	N/A	41/123 (33%)	43/128 (34%)

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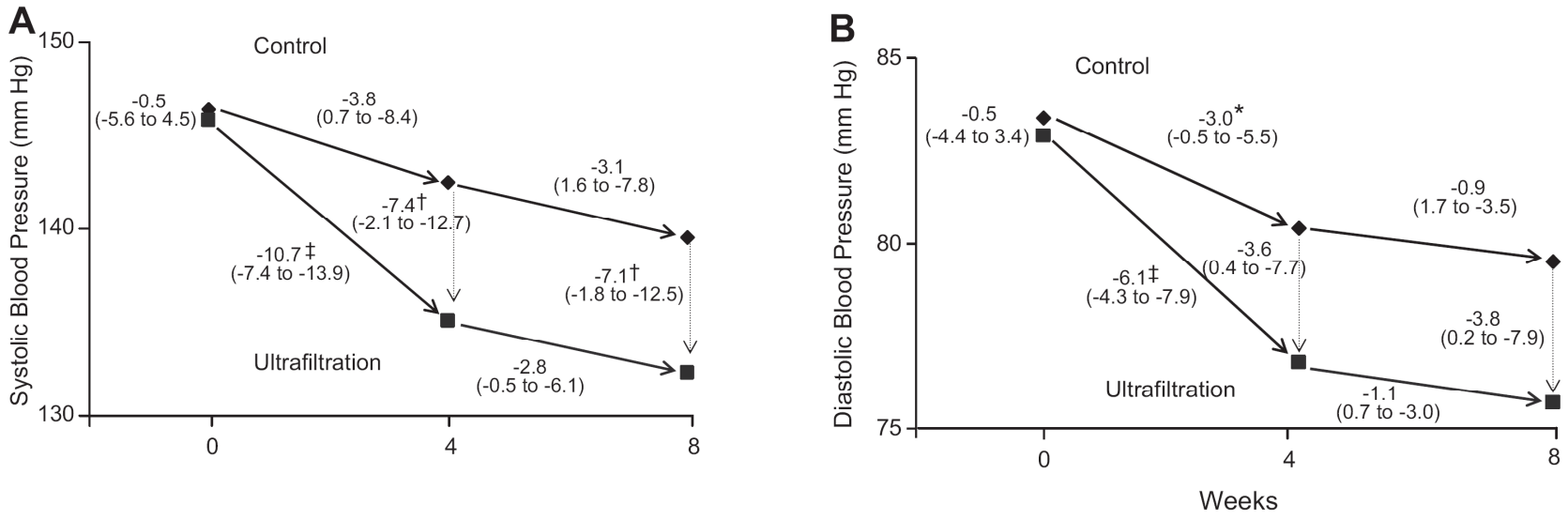
The effect of dry weight reduction on interdialytic ambulatory systolic and diastolic BP in hypertensive hemodialysis pts.



Agarwal et al. Hypertension 2009; 53: 500-507

Major problems before randomized prospective trials

- What is (are) the blood pressure measurement(s) a diagnosis of hypertension is based upon ?
- Do we have to subclassify according to heart failure (or other) ?
- How to account for „time on dialysis“ ?
- Role of dialysis regime ?

Pharmacologic properties of β-blockers in chronic dialysis patients

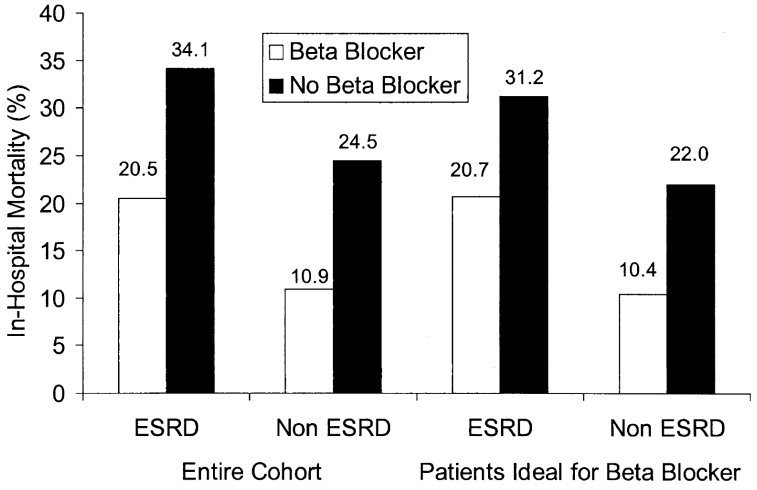
	T1/2(h) normal	T1/2(h) ESRD	Initial dose in HD	Maintenance dose in HD	Removal during HD
Acebutolol	3.5	3.5	200 q24h	200-300 q24h	yes
Atenolol	6-9	<120	25 q48h	25-50 q48h	Yes
Carvedilol	4-7	4-7	5 q24h	5 q24h	no
Metoprolol	3-4	3-4	50 b.i.d.	50-100 b.i.d.	high
Propranolol	2-4	2-4	40 b.i.d.	40-80 b.i.d.	yes

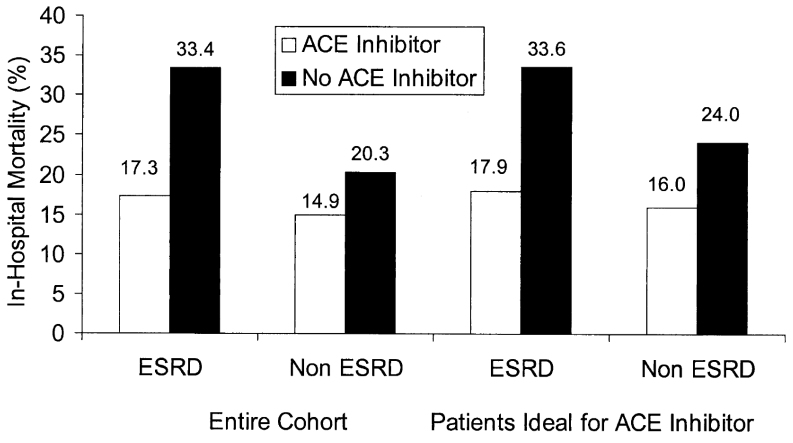
Henrich W. Principles and Practice of Dialysis

Observational studies of beta blockers

ESRD Database + Cooperative Cardiovascular Project Database

Association of medication classes with 30-day mortality after Myocardial infarction in pts with ESRD





Berger et al. JACC 2003;42:201-208

Pharmacokinetic properties of ACE Inhibitors in ESRD

	T1/2(h) normal	T1/2(h) ESRD	Initial dose in HD	Maintenance dose in HD	Removal during HD
Captopril	2-3	20-30	12.5 q24h	25-50 q24h	Yes
Enalapril	11	prolonged	2.5 q24h or q48h	2.5-10 q24h or q48h	Yes
Fosinopril	12	prolonged	10 q24h	10-20 q24h	Yes
Lisinopril	13	54	2.5 q24h or q48h	2.5-10 q24h or q48h	Yes
Ramipril	11	prolonged	2.5-5q24h	2.5-10 q24h	yes

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Pharmacokinetic properties of ARB's in ESRD

	T1/2(h) normal	T1/2(h) ESRD	Initial dose in HD	Maintenance dose in HD	Removal during HD
Candesartan	9	?	4 q24h	8-32 q24h	No
Irbesartan	11-15	11-15	75-150 q24h	150-300 q24h	No
Losartan	2	4	50 q24h	50-100 q24h	No
Telmisartan	24	?	40 q24h	20-80 q24h	No
Valsartan	6	?	80 q24h	80-160 q24h	No

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